WEST Search History

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DATE: Tuesday, April 18, 2006

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,EPAB; PLUR=YES; OP=ADJ	
☐	L34	L33 not @ay>2001	4
☐	L33	L3 and L21	63
☐	L32	L31 and L26	4
☐	L31	L30 and L24	667
☐	L30	stabil$	1066686
☐	L29	L19 and L24	20
☐	L28	L26 and L21	4
☐	L27	L26 abd k21	0
☐	L26	L16.ab.	295
☐	L25	s L17.ab.	1
☐	L24	L21 and L16	768
☐	L23	L21 and L19	20
☐	L22	L21 and L20	23
☐	L21	ewing$ NEAR2 sarcoma	2014
☐	L20	zyxin	181
☐	L19	cofilin	216
☐	L18	L17 and L14	3
☐	L17	actin	26040
☐	L16	actin	26040
☐	L15	L14 and L13	2
☐	L14	(auclair or amsellem or hervy or subra).in.	337
☐	L13	L12 or L11 or L10	22041
☐	L12	(435/7.23)![CCLS]	3264
☐	L11	(424/93.21)![CCLS]	1908
☐	L10	(514/12 |514/44 |514/9)![CCLS]	17734
☐	L9	L8 AND L3	1
☐	L8	20040191230.pn.	1
☐	L7	L5 not @ay>2001	4
☐	L6	L5 not @py>2001	0
☐	L5	L4 and sarcoma	83
☐	L4	L3 and ewing$	83

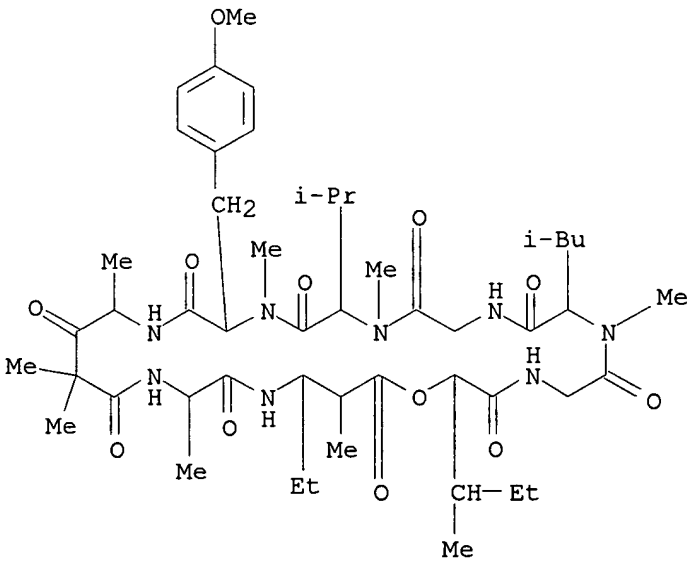
☐	L3	jasplakinolide	201
☐	L2	L1 and ewing$	1
☐	L1	dolastatin 11	11

END OF SEARCH HISTORY

RN 111517-68-1 REGISTRY
CN Cyclo[L-alanyl-(2S,3R)-3-amino-2-methylpentanoyl-(2S,3S)-2-hydroxy-3-methylpentanoylglycyl-N-methyl-L-leucylglycyl-N-methyl-L-valyl-N,O-dimethyl-L-tyrosyl-(4S)-4-amino-2,2-dimethyl-3-oxopentanoyl] (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Oxa-4,7,10,13,16,19,24,27-octaazacyclotriacontane, cyclic peptide deriv.
CN **Dolastatin 11**
OTHER NAMES:
CN NSC 606195
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 8
NTE modified (modifications unspecified)

type	------ location ------		description
bridge	Gly-1	- Oaa-8	covalent bridge
uncommon	Oaa-6	-	-
uncommon	Oaa-8	-	-

SEQ 1 GLGVYXAX
MF C50 H80 N8 O12
SR CA
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, NAPRALERT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Dissertation; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: PREP (Preparation); PRP (Properties)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

22 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

22 REFERENCES IN FILE CAPLUS (1907 TO DATE)

CCESSION NUMBER: 2005:184733 CAPLUS
DOCUMENT NUMBER: 142:371546
TITLE: The actin cytoskeleton-associated protein **zyxin** acts as a tumor suppressor in **Ewing** tumor cells
AUTHOR(S): Amsellem, Valerie; Kryszke, Marie-Helene; Hervy, Martial; Subra, Frederic; Athman, Rafika; Leh, Herve; Brachet-Ducos, Corinne; Auclair, Christian
CORPORATE SOURCE: CNRS UMR 8113, Laboratoire de Biotechnologie et Pharmacologie genetique appliquee, Ecole Normale Superieure de Cachan, Cachan, 94230, Fr.
SOURCE: Experimental Cell Research (2005), 304(2), 443-456
CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:583223 CAPLUS
DOCUMENT NUMBER: 141:188806
TITLE: Molecular mechanisms of CD99-induced caspase-independent cell death and cell-cell adhesion in **Ewing**'s sarcoma cells: actin and **zyxin** as key intracellular mediators
AUTHOR(S): Cerisano, Vanessa; Aalto, Yan; Perdichizzi, Stefania; Bernard, Ghislaine; Manara, Maria Cristina; Benini, Stefania; Cenacchi, Giovanna; Preda, Paola; Lattanzi, Giovanna; Nagy, Balint; Knuutila, Sakari; Colombo, Mario Paolo; Bernard, Alain; Picci, Piero; Scotlandi, Katia
CORPORATE SOURCE: Laboratorio di Ricerca Oncologica, Istituti Ortopedici Rizzoli, Bologna, 40136, Italy
SOURCE: Oncogene (2004), 23(33), 5664-5674
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 8	JAN 30	Saved answer limit increased
NEWS 9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 14	FEB 28	TOXCENTER reloaded with enhancements
NEWS 15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 16	MAR 01	INSPEC reloaded and enhanced
NEWS 17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 18	MAR 08	X.25 communication option no longer available after June 2006
NEWS 19	MAR 22	EMBASE is now updated on a daily basis
NEWS 20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS 22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS 23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS 25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

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NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

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FILE 'HOME' ENTERED AT 14:41:45 ON 17 APR 2006

=> file reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'REGISTRY' ENTERED AT 14:41:55 ON 17 APR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 16 APR 2006 HIGHEST RN 880543-27-1
DICTIONARY FILE UPDATES: 16 APR 2006 HIGHEST RN 880543-27-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> E "DOLASTATIN"/CN 25
E1 1 DOLASETRON MESYLATE/CN
E2 1 DOLASTANE/CN
E3 0 --> DOLASTATIN/CN
E4 1 DOLASTATIN 1/CN
E5 1 DOLASTATIN 10/CN
E6 1 DOLASTATIN 11/CN
E7 1 DOLASTATIN 12/CN
E8 1 DOLASTATIN 13/CN
E9 1 DOLASTATIN 13,
4-(3-AMINO-3,4-DIHYDRO-2-OXO-A-(PHENYLMETHYL)-1(2H)-PYRIDINEACETIC ACID)-/CN
E10 1 DOLASTATIN 13,
4-(3-AMINO-3,4-DIHYDRO-6-HYDROXY-2-OXO-A-(PHENYLMETHYL)-1(2H)-PYRIDINEACETIC ACID)-/CN

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E11          1     DOLASTATIN 14/CN
E12          1     DOLASTATIN 15/CN
E13          1     DOLASTATIN 16/CN
E14          1     DOLASTATIN 17/CN
E15          1     DOLASTATIN 17 (DOLABELLA AURICULARIA)/CN
E16          1     DOLASTATIN 18/CN
E17          1     DOLASTATIN 19/CN
E18          1     DOLASTATIN 2/CN
E19          1     DOLASTATIN 3/CN
E20          1     DOLASTATIN 4/CN
E21          1     DOLASTATIN 5/CN
E22          1     DOLASTATIN 6/CN
E23          1     DOLASTATIN 7/CN
E24          1     DOLASTATIN 8/CN
E25          1     DOLASTATIN 9/CN

=> S E6
L1           1 "DOLASTATIN 11"/CN

=> DIS L1 1 SQIDE
THE ESTIMATED COST FOR THIS REQUEST IS 6.36 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   111517-68-1  REGISTRY
CN   Cyclo[L-alanyl-(2S,3R)-3-amino-2-methylpentanoyl-(2S,3S)-2-hydroxy-3-
     methylpentanoylglycyl-N-methyl-L-leucylglycyl-N-methyl-L-valyl-N,O-
     dimethyl-L-tyrosyl-(4S)-4-amino-2,2-dimethyl-3-oxopentanoyl] (9CI)  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   1-Oxa-4,7,10,13,16,19,24,27-octaazacyclotriacontane, cyclic peptide deriv.
CN   Dolastatin 11
OTHER NAMES:
CN   NSC 606195
FS   PROTEIN SEQUENCE; STEREOSEARCH
SQL  8
NTE  modified (modifications unspecified)
-----------------------------------------------------------------------
 type            ------ location ------         description
-----------------------------------------------------------------------
bridge           Gly-1       - Oaa-8       covalent bridge
uncommon         Oaa-6           -         -
uncommon         Oaa-8           -         -
-----------------------------------------------------------------------

SEQ      1 GLGVYXAX
MF   C50 H80 N8 O12
SR   CA
LC   STN Files:   BEILSTEIN*, BIOSIS, CA, CAPLUS, NAPRALERT, TOXCENTER,
       USPATFULL
         (*File contains numerically searchable property data)
DT.CA  CAplus document type:  Dissertation; Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); PROC (Process); PRP
       (Properties); USES (Uses)
RL.NP  Roles from non-patents:  BIOL (Biological study); PREP (Preparation);
       PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents:  PREP
       (Preparation); PRP (Properties)
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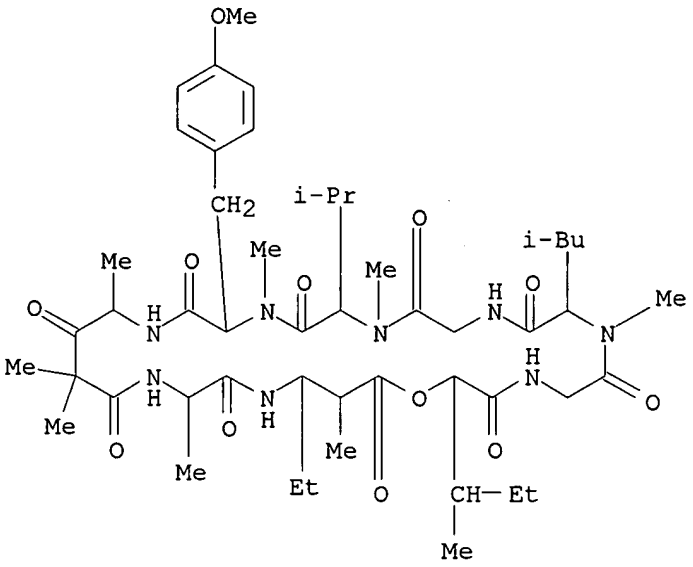

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

22 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
22 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> DIS L1 1 SQIDE
THE ESTIMATED COST FOR THIS REQUEST IS 6.36 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:N
REQUEST CANCELED

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	12.00	12.21

FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006
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FILE COVERS 1907 - 17 Apr 2006 VOL 144 ISS 17
FILE LAST UPDATED: 16 Apr 2006 (20060416/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
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http://www.cas.org/infopolicy.html

```
=> s actin
         49670 ACTIN
         30327 ACTINS
L2       52669 ACTIN
                (ACTIN OR ACTINS)

=> s cofilin
           775 COFILIN
           232 COFILINS
L3         812 COFILIN
                (COFILIN OR COFILINS)

=> s antag? or inhibit?
        281605 ANTAG?
       1822219 INHIBIT?
L4     1968300 ANTAG? OR INHIBIT?

=> s l4 (l) l3
L5         222 L4 (L) L3

=> s ewing?
L6        1659 EWING?

=> s l6 and l5
L7           1 L6 AND L5

=> d ibib

L7   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2002:977858  CAPLUS
DOCUMENT NUMBER:          138:52333
TITLE:                    Pharmaceutical composition for diagnosis, prevention
                          or treatment of a tumorous state, comprising a
                          modulator of the actin polymerization state
INVENTOR(S):              Auclair, Christian; Amsellem, Valerie; Hervy, Martial;
                          Subra, Frederic
PATENT ASSIGNEE(S):       Bioalliance Pharma, Fr.; Ecole Normale Superieure De
                          Cachan; Institut Gustave Roussy-IGR; Centre National
                          de la Recherche Scientifique CNRS
SOURCE:                   PCT Int. Appl., 68 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2002102846         A2    20021227    WO 2002-FR2106           20020618
     WO 2002102846         A3    20040422
     WO 2002102846         B1    20040603
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
             GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
             GN, GQ, GW, ML, MR, NE, SN, TD, TG
     FR 2825928            A1    20021220    FR 2001-7976             20010618
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     FR 2825928           B1    20040402
     CA 2450845           AA    20021227    CA 2002-2450845        20020618
     EP 1432732           A2    20040630    EP 2002-745538         20020618
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2005504521        T2    20050217    JP 2003-506318         20020618
     US 2004191230        A1    20040930    US 2003-740266         20031218
PRIORITY APPLN. INFO.:                      FR 2001-7976        A  20010618
                                            WO 2002-FR2106      W  20020618


=> s l1
L8          22 L1

=> s l8 and l6
L9           0 L8 AND L6

=> s zyxin
           219 ZYXIN
            28 ZYXINS
L10        224 ZYXIN
                (ZYXIN OR ZYXINS)

=> s l10 and l6
L11          3 L10 AND L6

=> d ibib 1-3

L11  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2005:184733  CAPLUS
DOCUMENT NUMBER:         142:371546
TITLE:                   The actin cytoskeleton-associated protein
                         zyxin acts as a tumor suppressor in
                         Ewing tumor cells
AUTHOR(S):               Amsellem, Valerie; Kryszke, Marie-Helene; Hervy,
                         Martial; Subra, Frederic; Athman, Rafika; Leh, Herve;
                         Brachet-Ducos, Corinne; Auclair, Christian
CORPORATE SOURCE:        CNRS UMR 8113, Laboratoire de Biotechnologie et
                         Pharmacologie genetique appliquee, Ecole Normale
                         Superieure de Cachan, Cachan, 94230, Fr.
SOURCE:                  Experimental Cell Research (2005), 304(2), 443-456
                         CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER:               Elsevier
DOCUMENT TYPE:           Journal
LANGUAGE:                English
REFERENCE COUNT:         54    THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11  ANSWER 2 OF 3  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2004:583223  CAPLUS
DOCUMENT NUMBER:         141:188806
TITLE:                   Molecular mechanisms of CD99-induced
                         caspase-independent cell death and cell-cell adhesion
                         in Ewing's sarcoma cells: actin and
                         zyxin as key intracellular mediators
AUTHOR(S):               Cerisano, Vanessa; Aalto, Yan; Perdichizzi, Stefania;
                         Bernard, Ghislaine; Manara, Maria Cristina; Benini,
                         Stefania; Cenacchi, Giovanna; Preda, Paola; Lattanzi,
                         Giovanna; Nagy, Balint; Knuutila, Sakari; Colombo,
                         Mario Paolo; Bernard, Alain; Picci, Piero; Scotlandi,
                         Katia
CORPORATE SOURCE:        Laboratorio di Ricerca Oncologica, Istituti Ortopedici
                         Rizzoli, Bologna, 40136, Italy
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SOURCE: Oncogene (2004), 23(33), 5664-5674
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:977858 CAPLUS
DOCUMENT NUMBER: 138:52333
TITLE: Pharmaceutical composition for diagnosis, prevention or treatment of a tumorous state, comprising a modulator of the actin polymerization state
INVENTOR(S): Auclair, Christian; Amsellem, Valerie; Hervy, Martial; Subra, Frederic
PATENT ASSIGNEE(S): Bioalliance Pharma, Fr.; Ecole Normale Superieure De Cachan; Institut Gustave Roussy-IGR; Centre National de la Recherche Scientifique CNRS
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102846	A2	20021227	WO 2002-FR2106	20020618
WO 2002102846	A3	20040422		
WO 2002102846	B1	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2825928	A1	20021220	FR 2001-7976	20010618
FR 2825928	B1	20040402		
CA 2450845	AA	20021227	CA 2002-2450845	20020618
EP 1432732	A2	20040630	EP 2002-745538	20020618
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JP 2005504521	T2	20050217	JP 2003-506318	20020618
US 2004191230	A1	20040930	US 2003-740266	20031218
PRIORITY APPLN. INFO.:			FR 2001-7976 A	20010618
			WO 2002-FR2106 W	20020618

=> d his

(FILE 'HOME' ENTERED AT 14:41:45 ON 17 APR 2006)

FILE 'REGISTRY' ENTERED AT 14:41:55 ON 17 APR 2006
E "DOLASTATIN"/CN 25
L1 1 S E6

FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006
L2 52669 S ACTIN

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L3          812 S COFILIN
L4      1968300 S ANTAG? OR INHIBIT?
L5          222 S L4 (L) L3
L6         1659 S EWING?
L7            1 S L6 AND L5
L8           22 S L1
L9            0 S L8 AND L6
L10         224 S ZYXIN
L11           3 S L10 AND L6

=> s l3 and l6
L12           6 L3 AND L6

=> s l12 and l4
L13           4 L12 AND L4

=> d ibib 1-4

L13  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:248644  CAPLUS
DOCUMENT NUMBER:          142:274057
TITLE:                    Sequences of human schizophrenia related genes and use
                          for diagnosis, prognosis and therapy
INVENTOR(S):              Liew, Choong-chin
PATENT ASSIGNEE(S):       Chondrogene Limited, Can.
SOURCE:                   U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S.
                          Ser. No. 802,875.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   47
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     US 2004241727         A1    20041202    US 2004-812731           20040330
     US 2004014059         A1    20040122    US 2002-268730           20021009
     US 2005191637         A1    20050901    US 2004-803737           20040318
     US 2005196762         A1    20050908    US 2004-803759           20040318
     US 2005196763         A1    20050908    US 2004-803857           20040318
     US 2005196764         A1    20050908    US 2004-803858           20040318
     US 2005208505         A1    20050922    US 2004-803648           20040318
     US 2004241727         A1    20041202    US 2004-812731           20040330
PRIORITY APPLN. INFO.:                       US 1999-115125P      P   19990106
                                             US 2000-477148       B1  20000104
                                             US 2002-268730       A2  20021009
                                             US 2003-601518       A2  20030620
                                             US 2004-802875       A2  20040312
                                             US 2004-812731       A   20040330

L13  ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:248643  CAPLUS
DOCUMENT NUMBER:          142:274056
TITLE:                    Sequences of human schizophrenia related genes and use
                          for diagnosis, prognosis and therapy
INVENTOR(S):              Liew, Choong-Chin
PATENT ASSIGNEE(S):       Chondrogene Limited, Can.
SOURCE:                   U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S.
                          Ser. No. 802,875.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   47
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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004241727	A1	20041202	US 2004-812731		20040330
US 2004014059	A1	20040122	US 2002-268730		20021009
US 2005191637	A1	20050901	US 2004-803737		20040318
US 2005196762	A1	20050908	US 2004-803759		20040318
US 2005196763	A1	20050908	US 2004-803857		20040318
US 2005196764	A1	20050908	US 2004-803858		20040318
US 2005208505	A1	20050922	US 2004-803648		20040318
US 2004241727	A1	20041202	US 2004-812731		20040330
PRIORITY APPLN. INFO.:			US 1999-115125P	P	19990106
			US 2000-477148	B1	20000104
			US 2002-268730	A2	20021009
			US 2003-601518	A2	20030620
			US 2004-802875	A2	20040312
			US 2004-812731	A	20040330

L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:60754 CAPLUS
Correction of: 2004:1036571
DOCUMENT NUMBER: 142:233342
Correction of: 142:16836
TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 29
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004241727	A1	20041202	US 2004-812731		20040330
US 2004014059	A1	20040122	US 2002-268730		20021009
US 2005191637	A1	20050901	US 2004-803737		20040318
US 2005196762	A1	20050908	US 2004-803759		20040318
US 2005196763	A1	20050908	US 2004-803857		20040318
US 2005196764	A1	20050908	US 2004-803858		20040318
US 2005208505	A1	20050922	US 2004-803648		20040318
US 2004265869	A1	20041230	US 2004-812716		20040330
US 2005208519	A1	20050922	US 2004-989191		20041115
PRIORITY APPLN. INFO.:			US 1999-115125P	P	19990106
			US 2000-477148	B1	20000104
			US 2002-268730	A2	20021009
			US 2003-601518	A2	20030620
			US 2004-802875	A2	20040312
			US 2004-812731	A2	20040330
			WO 2004-US20836	A2	20040621

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:977858 CAPLUS
DOCUMENT NUMBER: 138:52333
TITLE: Pharmaceutical composition for diagnosis, prevention or treatment of a tumorous state, comprising a modulator of the actin polymerization state
INVENTOR(S): Auclair, Christian; Amsellem, Valerie; Hervy, Martial; Subra, Frederic

PATENT ASSIGNEE(S): Bioalliance Pharma, Fr.; Ecole Normale Superieure De Cachan; Institut Gustave Roussy-IGR; Centre National de la Recherche Scientifique CNRS
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002102846	A2	20021227	WO 2002-FR2106		20020618
WO 2002102846	A3	20040422			
WO 2002102846	B1	20040603			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
FR 2825928	A1	20021220	FR 2001-7976		20010618
FR 2825928	B1	20040402			
CA 2450845	AA	20021227	CA 2002-2450845		20020618
EP 1432732	A2	20040630	EP 2002-745538		20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2005504521	T2	20050217	JP 2003-506318		20020618
US 2004191230	A1	20040930	US 2003-740266		20031218
PRIORITY APPLN. INFO.:			FR 2001-7976	A	20010618
			WO 2002-FR2106	W	20020618

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L1             1 S E6

     FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006
L2         52669 S ACTIN
L3           812 S COFILIN
L4       1968300 S ANTAG? OR INHIBIT?
L5           222 S L4 (L) L3
L6          1659 S EWING?
L7             1 S L6 AND L5
L8            22 S L1
L9             0 S L8 AND L6
L10          224 S ZYXIN
L11            3 S L10 AND L6
L12            6 S L3 AND L6
L13            4 S L12 AND L4

=> s phosphoinositol?
L14          989 PHOSPHOINOSITOL?

=> s l14 and l6
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L15           0 L14 AND L6

=> s phosphotidylinositol
            96 PHOSPHOTIDYLINOSITOL
             2 PHOSPHOTIDYLINOSITOLS
L16         98 PHOSPHOTIDYLINOSITOL
                (PHOSPHOTIDYLINOSITOL OR PHOSPHOTIDYLINOSITOLS)

=> s l15 and l6
L17           0 L15 AND L6

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    29.78      41.99

FILE 'PCTFULL' ENTERED AT 14:49:15 ON 17 APR 2006
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FILE LAST UPDATED:          11 APR 2006      <20060411/UP>
MOST RECENT UPDATE WEEK:        200614        <200614/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
    SEE
    http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE
    (last updated April 10, 2006) <<<

=> s cofilin
           179 COFILIN
            12 COFILINS
L18        188 COFILIN
                (COFILIN OR COFILINS)

=> s ewing?
L19       3185 EWING?

=>

=> s l19 and l18
L20          19 L19 AND L18

=> s antag? or inhibit?
         53720 ANTAG?
        189862 INHIBIT?
L21     198141 ANTAG? OR INHIBIT?

=> s l20 and l21
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=> s l22 not py>2001
        488865 PY>2001
L23           4 L22 NOT PY>2001

=> d ibib 1-4

L23    ANSWER 1 OF 4     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2001055168 PCTFULL  ED 20020827
TITLE (ENGLISH):         NUCLEIC ACIDS, PROTEINS AND ANTIBODIES
```

TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES, ET ANTICORPS

INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.

PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055168	A1	20010802

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-US1331 A 20010117

PRIORITY INFO.:

US 2000-60/179,065	20000131
US 2000-60/180,628	20000204
US 2000-60/184,664	20000224
US 2000-60/186,350	20000302
US 2000-60/189,874	20000316
US 2000-60/190,076	20000317
US 2000-60/198,123	20000418
US 2000-60/205,515	20000519
US 2000-60/209,467	20000607
US 2000-60/214,886	20000628
US 2000-60/215,135	20000630
US 2000-60/216,647	20000707
US 2000-60/216,880	20000707
US 2000-60/217,487	20000711
US 2000-60/217,496	20000711
US 2000-60/218,290	20000714
US 2000-60/220,963	20000726
US 2000-60/220,964	20000726
US 2000-60/225,757	20000814
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US 2000-60/225,447	20000814
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US 2000-60/225,213	20000814
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US 2000-60/224,519	20000814
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US 2000-60/225,268	20000814
US 2000-60/225,758	20000814
US 2000-60/225,267	20000814
US 2000-60/225,214	20000814
US 2000-60/226,279	20000818
US 2000-60/226,868	20000822
US 2000-60/227,182	20000822
US 2000-60/226,681	20000822
US 2000-60/227,009	20000823
US 2000-60/228,924	20000830
US 2000-60/229,344	20000901
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US 2000-60/229,345	20000901

US 2000-60/229,513	20000905
US 2000-60/229,509	20000905
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US 2000-60/230,437	20000906
US 2000-60/231,413	20000908
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US 2000-60/231,244	20000908
US 2000-60/231,414	20000908
US 2000-60/232,080	20000908
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US 2000-60/235,834	20000927
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US 2000-60/236,368	20000929
US 2000-60/236,370	20000929
US 2000-60/236,327	20000929
US 2000-60/237,039	20001002
US 2000-60/237,038	20001002
US 2000-60/237,040	20001002
US 2000-60/237,037	20001002
US 2000-60/236,802	20001002
US 2000-60/239,937	20001013
US 2000-60/239,935	20001013
US 2000-60/241,221	20001020
US 2000-60/241,808	20001020
US 2000-60/241,787	20001020
US 2000-60/240,960	20001020
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US 2000-60/244,617	20001101
US 2000-60/246,474	20001108
US 2000-60/246,532	20001108
US 2000-60/246,609	20001108
US 2000-60/246,613	20001108
US 2000-60/246,610	20001108
US 2000-60/246,611	20001108
US 2000-60/246,477	20001108
US 2000-60/246,527	20001108
US 2000-60/246,528	20001108
US 2000-60/246,525	20001108
US 2000-60/246,475	20001108
US 2000-60/246,526	20001108
US 2000-60/246,476	20001108
US 2000-60/246,478	20001108
US 2000-60/246,523	20001108

US 2000-60/246,524	20001108
US 2000-60/249,299	20001117
US 2000-60/249,297	20001117
US 2000-60/249,244	20001117
US 2000-60/249,245	20001117
US 2000-60/249,207	20001117
US 2000-60/249,212	20001117
US 2000-60/249,213	20001117
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US 2000-60/249,211	20001117
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US 2000-60/250,160	20001201
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US 2000-60/256,719	20001205
US 2000-60/251,030	20001205
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US 2000-60/251,479	20001206
US 2000-60/251,869	20001208
US 2000-60/251,856	20001208
US 2000-60/251,868	20001208
US 2000-60/251,990	20001208
US 2000-60/251,989	20001208
US 2000-60/254,097	20001211
US 2001-60/259,678	20010105

L23 ANSWER 2 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 1999051766 PCTFULL ED 20020515

TITLE (ENGLISH): METHODS FOR PRODUCING LIBRARIES OF EXPRESSIBLE GENE SEQUENCES

TITLE (FRENCH): METHODES DE PRODUCTION DE BANQUES DE SEQUENCES DE GENES EXPRIMABLES

INVENTOR(S): FERNANDEZ, Joseph, Manuel;
HEYMAN, John, Alastair;
HOEFFLER, James, Paul;
MARKS-HULL, Heather, Lynn;
SINDICI, Michelle, Lynn

PATENT ASSIGNEE(S): INVITROGEN;
FERNANDEZ, Joseph, Manuel;
HEYMAN, John, Alastair;
HOEFFLER, James, Paul;
MARKS-HULL, Heather, Lynn;
SINDICI, Michelle, Lynn

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9951766	A1	19991014

DESIGNATED STATES W: AU CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.: WO 1999-US7270 A 19990402

PRIORITY INFO.: US 1998-09/054,936 19980403

L23 ANSWER 3 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999051620 PCTFULL ED 20020515
TITLE (ENGLISH): LIBRARIES OF EXPRESSIBLE GENE SEQUENCES
TITLE (FRENCH): BANQUES DE SEQUENCES DE GENES POUVANT ETRE EXPRIMEES
INVENTOR(S): FERNANDEZ, Joseph, Manuel;
HEYMAN, John, Alastair;
HOEFFLER, James, Paul
PATENT ASSIGNEE(S): INVITROGEN
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9951620	A1	19991014

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1999-US7334 A 19990402
PRIORITY INFO.: US 1998-60/080,626 19980403
US 1998-60/096,981 19980818

L23 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1998041648 PCTFULL ED 20020514
TITLE (ENGLISH): TARGET GENES FOR ALLELE-SPECIFIC DRUGS
TITLE (FRENCH): GENES CIBLES POUR MEDICAMENTS SPECIFIQUES D'ALLELES
INVENTOR(S): HOUSMAN, David;
LEDLEY, Fred, D.;
STANTON, Vincent, P., Jr.
PATENT ASSIGNEE(S): VARIAGENICS, INC.;
HOUSMAN, David;
LEDLEY, Fred, D.;
STANTON, Vincent, P., Jr.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9841648	A2	19980924

DESIGNATED STATES
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-US5419 A 19980319
PRIORITY INFO.: US 1997-60/041,057 19970320

=> d kwic 2

L23 ANSWER 2 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . U3 52.36 60
snoRNP associated 55 kDa
protein
GI H-DO0096 Transtyretin (prealbumin) 16.28 20
C4 H-DO0408 Cytochrome P450 IIIA7 (P450- 55.44 64
HFLa)
M302 E7 H-DO0682 **cofilin** 18.37 30
M383 G2 H-DO0726 ferrochelatase 46.64 50.OkDa
M383 C3 H-DO0760 proteasome, subunit HO 25.85 34.OkDa
M305 B4 H-DO0761 proteasome, subunit HC5 26.62. . .
. . .

enoyl-Coenzyme A hydratase, 32.01 58
short chain, mitochondrial
El H-DI4446 Human HFREP- I mRNA for 34.43 40
unknown protein, complete cds
167-14 H-DI4497 H.sapiens (**Ewing**'s sarcoma cell 51.44 64
line) mRNA encoding open
reading frame
M266 D2 H-DI4520 basic transcription element- 24.2 33.OkDa
binding protein 2
M318 D2 H-DI4658 hypothetical. . .
. . .
42.79 48
M298 C2 H-JO2611 apolipoprotein D 20.9 3 I.OkDa
M266 C4 H-JO2683 ADP/ATP carrier protein 32.89 36
M383 H2 H-JO2685 plasminogen activator **inhibitor**, 45.76
50.OkDa
placenta
167-3 H-JO2853 casein kinase 11, alpha chain 43.08 50
E3 H-JO2854 Human 20-kDa myosin light 19.03 31
chain (MLC-2) mRNA, complete
cds
M248. . .
. . .
transaldolase 37.18 39.OkDa
M423 C4 H-LI9593 Interleukin 8 receptor, beta 39.71 4 1.0kDa
G I H-LI9686 Homo sapiens macrophage 12.76 1 3
migration **inhibitory** factor (MIF)
gene, complete cds
G2 H-LI9739 metallopanstimulin 1 9.35 32
M302 E3 H-LI9871 activating transcription factor 3 20.02 36.OkDa
167-86 H-L20422 14 3 protein eta 34 1 3
M440 B2 H-L20492 Human garmna-glutamyl 24.86 35.OkDa
transpeptidase mRNA, complete
cds
M315 BI H-L20688 GDP-dissociation **inhibitor** 22.22 32
protein rhoA
M271 H3 H-L20941 ferritin, heavy polypeptide. 20.24 32
FERRITIN IS AN
INTRACELLULAR,
MOLECULE THAT STORES
IRON IN A SOLUBLE,
NONTOXIC, READILY
AVAILABLE FORM.
. . .
30
transforming protein rhoC,
Aplysia ras-related hornolog 9
M236 E3 H-L25085 Sec6l complex, beta subunit, 10.67 19
PROTEIN TRANSLOCATION
TN THE ENDOPLASMIC
RETICULUM
167-85 H-1,25610 cyclin-dependent kinase **inhibitor** 32
B2 H-L25610 cyclin-dependent kinase **inhibitor** 18.110 40
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M297 H2 H-1,26232 cathepsin A/phospholipid transfer 54.34 64.OkDa
protein
167-4 H-1,26318 stress-activated protein kinase 52 42.31
JNKI
M428 Fl H-1,27586 Human TR4 orphan. . .
. . .
E2 H-MI9713 tropomyosin, alpha, muscle 31.35 4I.OkDa
167-79 H-MI9722 proto-oncogene tyrosine-protein 64 58.26
kinase FGR

M248 HI H-M20560 Annexin III (lipocortin III), 35.64 37
INHIBITOR OF
PHOSPHOLIPASE A2
M235 HI H-M20681 GLUCOSE TRANSPORTER 54.67 50
TYPE 3, BRAIN
167-29 H-M21616 beta platelet-derived growth 121 121.7
factor receptor precursor
M305 A3 H-M21812. . .
. . .
palmitoylated membrane protein, 51.37 5 I.OkDa
erythrocyte, 55 kDa
M302 C7 H-M65292 complement factor H-related 36.41 50
protein (GB:M65292)
D3 H-M68516 Human protein C **inhibitor** gene, 44.77 54
complete cds
167-27 H-M68520 cell division protein kinase 2 38 32.85
M236 D5 H-M68867 Cellular retinoic acid-binding 15.29 19.OkDa
protein 2,. . .
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Al H-PO 197 S-adenosyhnethionine synthetase 42.46
2 (metX)
M365 BI H-PO203 hypothetical protein 10.12
M365 Cl H-PO209 hypothetical protein 49.61
M365 DI H-PO213 glucose **inhibited** division protein 68.42
(gidA)
M381 El H-PO218 hypothetical protein 20.24
M365 El H-PO221 nifLJ-Iike protein 35.97
M365 F1 H-PO227 outer m mbrane protein (omp5). . . C2 P]3 -]]
ribosomal protein SI (rps 1)
M366 D2 H-PO403 phenylalanyl-tRNA synthetase, 36.19
alpha subunit (pheS)
M366 E2 H-PO404 protein kinase C **inhibitor** 11.55
(SP:PI6436)
M366 F2 H-PO405 nifS-like protein 48.51
M366 G2 H-PO406 hypothetical protein 21.67
M366 H2 H-PO407 biotin sulfoxide reductase (bisC) 87.67
M381 DI H-PO409. . .
. . .
alanine racemase, biosynthetic 41.58
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M371 D6 H-PO942 D-alanine glycine perinease 49.61
(dagA)
M371 E6 H-PO943 D-arnino acid dehydrogenase 45.21
(dadA)
M371 F6 H-PO944 translation initiation **inhibitor**, 13.86
putative
M371 G6 H-PO946 conserved hypothetical integral 54.67
membrane protein
M371 H6 H-PO947 hypothetical protein 13.31
M371 A7 H-PO949 conserved hypothetical secreted 16.61
protein
M371 B7. . .
. . .
factor Ile, 48.360
alpha subunit
M302 D7 H-S69022 myosin, light polypeptide 2, 18.26 3 1
ventricular
H5 H-S69272 cytoplasmic antiproteinase=38 41.47 50
kda intracellular serine proteinase
inhibitor [human, placenta,
mRNA, 1465 nt]
DI H-S72043 GIF=growth **inhibitory** factor 7.59 19
[human, brain, Genornic, 2015 nt]

M266 B3 H-S74221 cytokine lK factor 17.93 36.OkDa
DI H-S74445 cellular retinoic acid-binding 15.18 23
protein. . . small nuclear ribonucleoprotein, 13.97 17.OkDa
Sm D3
M311 D4 H-UI6660 enoyl-Coenzyme A hydratase-like 36.19 38
protein, peroxisomal
M302 H4 H-UI7074 cyclin-dependent kinase 6 18.59 29
inhibitor p 1 8
M306 A2 H-UI7195 A-kinase anchor protein I 00 72.05 100
[AKAPIOO*]
DI -UI7280 Steroidogenic acute regulatory 31.46 35
protein
M316 171 H-UI8291. . .
. . .
29.15 38.OkDa
factor TAF1132 mRNA, complete
cds
M424 H3 H-U22662 Human nuclear orphan receptor 49.28 49.OkDa
LXR-alpha mRNA, complete cds
M271 D2 H-U24074 killer cell **inhibitory** receptor 37.62 43
[KIR], Homo sapiens natural
killer-associated transcript 3
(NKAT3), complete cds.
. . .
30
gamma
M416 D3 H-U26403 Human receptor tyrosine kinase 25.19 30.OkDa
ligand LERK-7 precursor
(EPLG7) mRNA, complete cds
M317 E2 H-U27143 human protein kinase C **inhibitor**- 13.900
17.OkDa
I cDNA
E5 H-U28249 Human II kd protein mRNA, 12.32 12
complete cds
F4 H-U28386 Human nuclear localization 58.3 54
sequence receptor hSRP. . . phosphatase 2A, 56.65 55.OkDa
regulatory subunit B' alpha- I
El H-U37529 Human substance P beta-PPT-A 14.3 22
mRNA, complete cds
M305 H5 H-U37547 apoptosis **inhibitor** 68.09 64
M424 D5 H-U38480 Human retinoid X receptor- 51.04 61.OkDa
gamma mRNA, complete cds
M270 F4 H-U38810 Human mab-21 cell fate-
determining protein. . . mRNA
M298 E4 H-U39945 human adenylate kinase 2 (adk2) 26.3633 38.OkDa
mRNA
166-38 H-U40282 human integrin-finked kinase 55 49.68
(ILK) mRNA
169-65 H-U40343 human CDK **inhibitor** p I 9INK4d 1 8 18. 33
mRNA
E2 H-U40705 Homo sapiens telomeric repeat 48.4 52
binding factor (TRF I) mRNA,
complete cds
166-50 H-U40989. . . E2 H-U47677 Human transcription factor E2F 1
48.18 53.OkDa
(E2FI) gene, promoter and
m421 H I H-U48707 Human protein phosphatase- 1 18.92 36.OkDa
inhibitor mRNA, complete cds
M302 B7 H-U49070 peptidyl-prolyl isomerase PIN I 18.04 28.OkDa
C1 H-U49188 Human placenta (Diff33) mRNA, 54.45 70
complete cds
M485 H2. . .
. . .

46.97 60.OkDa
phosphodiesterase (PDE4Q
mRNA, 4C-426 isoform,
complete cds
M306 F3 H-U66867 ubiquitin-conjugating enzyme E21 17.49 28
[UBE2I]
M416 E2 H-U681 11 Human protein phosphatase 22.66 37.OkDa
inhibitor 2 (PPP I R2) gene
F2 H-U68382 Mannosidase, alpha B, lysosomal 35.64 36
G2 H-U69141 Glutaryl-Coenzyme A 48.29 56
dehydrogenase
B2 H-U70660 Human copper. . . (HAHI) mRNA, complete
cds
M297 B2 H-U71374 peroxisomal membrane protein 40.15 40.OkDa
(Pexl3p)
M306 A3 H-U75272 progastricsin [PGC] 42.79 49.OkDa
A2 H-U75285 Homo sapiens apoptosis **inhibitor** 15.73 25
survivin gene, complete cds
B2 H-U77456 Human nucleosome assembly 41.36 50
protein 2 mRNA, complete cds
C2 H-U78294 Homo sapiens 15S-lipoxygenase 74.47. . . and VIIIa)
M302 B3 H-XO2751 proto-oncogene N-ras 20.9 25.OkDa
D3 H-XO2812 Human mRNA for transforming 43.12 50
growth factor-beta (TGF-beta)
M302 CI H-XO3124 tissue **inhibitor** of 22.88 T6.OkDa
metalloproteinase I
M362 BI H-XO3342 ribosornal protein L32 14.96 24.OkDa
M235 A2 H-XO3484 human mRNA for raf oncogene 71.350 73.OkDa
M318. . .
. . .
basic protein, 23 kDa 22.44 30.OkDa
M318 GI H-X57025 insulin-like growth factor 1 16.94 1 8
M305 F5 H-X57348 protein kinase C **inhibitor** 27.39 35.OkDa
M236 D6 H-X57351 interferon-induced protein 1-813 14.63 24
H3 H-X57352 interferon-induced protein 1-8U 14.74 38
M305 B6 H-X58079 S- I 00. . . 49
E2 H-X59357 Epstein-Barr virus small RNA- 14.19 36
associated protein
M236 D4 H-X59417 macropain, iota subunit, THE 27.17 36
INTERACTION OF CALPONIN
WITH ACTIN **INHIBITS**
ACTOMYOSIN MG-ATPASE
ACTIVITY
M271 H4 H-X59618 ribonucleotide reductase, small 42.9 46
subunit
M250 G3 H-X59710 CAAT-box DNA-binding protein, 22.66 34
subunit B, CCAAT-BINDING
TRANSCRIPTION FACTOR
SUBUNIT A [Homo. . .
. . .
H+ transporting, 42.13 58.OkDa
subunit C, vacuolar
M236 C3 H-X69392 ribosomal protein L26 16.06 29
B3 H-X69532 H.sapiens gene for inter-alpha- 100.32 98
trypsin **inhibitor** heavy chain HI,
exons 1-3
M236 F5 H-X69654 ribosomal protein S26 12.76 18
M421 C8 H-X70218 Protein phosphatase 4 (formerly 33.88
X), catalytic subunit
M266. . .

M235 BI H-X72841 Human retinoblastoma-binding 46.86 52.OkDa
protein (RbAp46) mRNA,

complete cds, IEF 7442
(GB:X72841)
217-25 H-X73428 DNA-binding protein **inhibitor** 20 17.08
ID-3
M305 B5 H-X73459 signal recognition particle, 15.07 20
subunit 14
M250 D6 H-X73460 ribosomal protein L3, isoform 2, 44.44 50.OkDa
COMPONENT OF. . .
. . .
H-YO0291 Human hap mRNA encoding a 49.39 59.OkDa
DNA-binding hormone receptor
M386 HI H-YO0345 polyadenylate-binding protein 69.74 70.OkDa
M469 A2 H-YO0630 Plasminogen activator **inhibitor**, 45.76
46.OkDa
type II (arginine-serpin)
M305 El H-YO0711 lactate dehydrogenase B 36.85 38.OkDa
H2 H-YO0764 ubiquinol/cytochrome c reductase 10.12 33
hinge protein
F5 H-YO7848 H.sapiens. . .

=> d kwic 4

L23 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ABEN . . . loss of one of these alleles in cancer cells due to loss of
heterozygosity (LOH) and (2) the
development of **inhibitors** with high specificity for the single
remaining alternative allele of the
essential gene retained by the tumor cell after LOH.. . .
ABFR . . . perte de l'un de ces alleles dans des cellules cancereuses, due a
la perte
d'heterozygotie (LOH); et (2) developper des **inhibiteurs**
presentant une specificite elevee pour
l'allele distinct restant du gene essentiel retenu par la cellule
tumorale apres LOH. Des categories. . .

DETD Specifically, this invention is concerned with target genes for drugs
that are useful
for treating such diseases by providing allele-specific
inhibition of essential cell
functions.
. . .
strategy for the development of anticancer agents having a high
therapeutic
232/116
index is described in Housman, International Application PCT/US/94 08473
and
Housman, **INHIBITORS** OF ALTERNATIVE ALLELES OF GENES
ENCODING PROTEINS VITAL FOR CELL VIABILITY OR CELL GROWTH
AS A BASIS FOR CANCER THERAPEUTIC AGENTS, U.S.. . . which undergo
loss of
heterozygosity in a cancer. Treatment of a cancer in an individual who
is
heterozygous with an allele specific **inhibitor** targeted to the
single allele of an
essential gene which is present in a cancer will **inhibit** the
growth of the cancer
cells. In contrast, the alternative allele present in non-cancerous
cells (which have
not undergone loss of heterozygosity). . .
. . .
(3) identification of the absence of one of these alleles in

cancer cells due to LOH and (4) development of specific **inhibitors** of the single remaining allele of the essential gene retained by the cancer cell, but not the alternative allele.

SUMMARY OF THE DWENTION

The utilization of **inhibitors** of alternative alleles, such as in the strategy described in Housman, supra, requires the provision of suitable target genes in order to identify such **inhibitors** and to implement corresponding diagnostic or therapeutic methods. Thus, as described below, the present invention identifies useful groups of genes which provide. . .

In each disease, the administration of such an **inhibitor** would have cytotoxic or antiproliferative effects on the abnormally proliferating cells that exhibited LOH and contained only the sensitive allele of the. . .

In addition, it was found that specific **inhibitors** of alternative alleles of an essential gene would be useful in managing transplantation in instances where the alleles in a donor bone marrow differ from the alleles in the recipient. For example, administration of an **inhibitor** of an allele that was present in a donor bone marrow but not the recipient could be used to treat graft-versus-host. . .

Alternatively, an **inhibitor** of an allele that is present in the recipient but not the donor bone marrow could be used to enhance engraftment by preferentially creating space in the recipient bone marrow for the graft without **inhibiting** proliferation of the engrafted donor marrow.

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The term target gene refers to a gene where the gene, its RNA transcript, or its protein product are specifically **inhibited** or potentially **inhibited** by a drug. In references herein to genes or alleles, the term encoding refers to the entire gene sequence, including both coding. . .

. . .

of alternative variances at a single variant site, or a combination of several different variances at different sites. In this invention, **inhibitors** targeted to a specific allelic form or subset of the allelic forms of a gene can be targeted to a specific variance. . .

. . .

dysplastic epithelium of lung, breast, cervix, or other tissues. Drugs used in treating cancer and other non-cancer proliferative disorders commonly aim to **inhibit** the proliferation of cells and are commonly referred to as antiproliferative agents.

. . .
particular sequence
variance. Also preferably, these terms refer to loss of heterozygosity of a
particular sequence variance that is recognized by an **inhibitor** that will **inhibit** one
allele of the gene present in normal cells of the individual, but not an alternative
allele.

. . .
the individual clones. The alleles subject to LOH may vary from one
clone to another. Therefore treatment of these conditions preferably utilizes
inhibitors of at least two allelic forms. Thus, methods relating to such disorders
can utilize alternative alleles of one gene and/or allelic. . .

. . .
of LOH in certain locations, for example segments of
chromosomes 7,8,10,11,13,16, and 18 in prostate cancer, administration of an
allele-specific drug that **inhibits** one allele that is within such a region, in a patient
who is heterozygous for alternative forms of the gene, would. . .

. . .
genes, and provides, as examples, specific genes within those categories
which are found to be suitable as targets for allele specific **inhibitors**, in particular
for killing cancer cells or reducing the proliferation of cells in cancer or noncancer
proliferative disorders. Thus, the present invention. . . more variant
positions, indicates that the gene is a useful potential target gene in this invention
for the identification of allele specific **inhibitors** and in other aspects of the
invention.

. . .
those skilled in the art) identifying the gene and providing a known
sequence) which can be used for identifying allele specific **inhibitors** and for use in
other aspects of this invention. Preferably the gene has the LOH frequency and at
least one sequence variance. . .

. . .
vital for cell viability or growth, or essential
for cell survival and proliferation have the same meaning. A gene is essential if
inhibition of the function of such a gene or gene product will kill the cell or **inhibit**
its growth as determined by methods known in the art. Growth **inhibition** can be
monitored as a reduction or preferably a cessation of cell proliferation.

. . .
the affected gene, genetic disruption of the gene by homologous recombination
or other methods in organisms ranging from yeast to mice, **inhibition** of the gene
by antisense oligonucleotides or ribozymes, and identification of the target of
known cytotoxic, drugs and other **inhibitors**. As further discussed below, the
essentiality of a gene can depend on the conditions to which the cell is

exposed.

. . .

entity is absent or present at low levels, the gene product is essential. In another example, the administration of a drug that **inhibits** one or more functions within the cell can cause other functions to be essential that are not essential in the absence. . .

. . .

Identification of one or more sequence variances in that gene and/or in the corresponding gene products allows screening or design of such **inhibitors** for potential treatment.

. . .

sequence variance, and therefore of individuals heterozygous for such variances, indicates that the gene can be used for the identification of **inhibitors** targeting allelic forms of the gene which have a particular variance or variances and in the other aspects of this invention.

. . .

gene is a potential target. The target gene, its RNA transcript or protein product can then be used as targets for allele-specific **inhibitors** for treating the proliferative disorder or other uses as described in the aspects of this invention.

. . .

of the population are heterozygous for that gene provides genes which are particularly likely to be useful target genes for allele specific **inhibition** in this invention.

. . .

or 50% of cases of such a disorder indicates that the gene is useful as a potential target for identifying allele specific **inhibitors** for the treatment of proliferative disorders and in other aspects of this 232/116 invention.

. . .

more preferably at least 30%, and most preferably at least 40% are heterozygous in a specific population that may be treated with **inhibitors** to treat cancer or other proliferative disorder in that population. Once a specific variance is identified in a certain gene, the. . .

In the context of this invention, an alternative allele, or other reference to an appropriate target for the **inhibitors** of this invention refers to a form of a gene which differs in base sequence from at least,one other allele or. . . no phenotypic effect on the physical condition of an individual having that variance until the variance is targeted by an allele specific **inhibitor** .

In connection with allele specific **inhibitors** and the methods of this invention, the

terms allelic form or alternative form of the target gene or sequence variance within the. . . either or both of the gene or a product of that gene including the RNA transcript or protein product. Thus, a particular
inhibitor may act in an allele specific manner (which will often be variance
specific) at any of those levels and preferably the **inhibitor** is targeted to a
particular sequence variance of the specific allelic form.

. . .

the classes described above in genes that are essential for cell survival or
proliferation that can be the targets for allele-specific **inhibitors** for the treatment
of cancer or noncancer proliferative disorders.

This invention provides **inhibitors** which are specific for at least one, but not all,
allelic forms of a gene that encodes a gene product essential to cell growth or cell
viability, for genes belonging to the specified categories of genes. The **inhibitor**
may be active on the gene or gene product including the RNA transcript, protein
product, or modifications thereof. Exposure to the **inhibitor** **inhibits** proliferation
or kills cells which have undergone LOH of genes that are not **inhibited** by the
drug and contain only an allelic form of the essential gene, its RNA transcript, or
its protein product against which the **inhibitor** is targeted. Normal cells which
contain two alternative alleles of the target genes, one of which is not **inhibited** by
the specific **inhibitor**, are spared from the toxic effects of the **inhibitor** because the
remaining activity of the allele which is not **inhibited** by the **inhibitor** is adequate
to permit continued cell viability and growth. This differential effect of the
inhibitor on cells with LOH of a targeted gene (e.g., a cancer cell) and normal
cells accounts for the high therapeutic index of the **inhibitors** of this invention for
the treatment of cancer or non-cancerous, proliferative disorders characterized by
LOH. Toxicity of the **inhibitor** to normal cells is therefore low, compared to most
currently available anticancer and antiproliferative agents.

. . .

indicated above and described
in the Detailed Description of the Preferred Embodiments, in a first aspect the
invention provides methods for identifying **inhibitors** potentially useful for
treatment of a proliferative disorder, e.g., cancer. Such **inhibitors** are active on
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specific allelic forms of target genes as identified herein. The method involves
determining at least two allelic forms of such a gene encoding an essential gene
product, and testing a potential allele specific **inhibitor** to

determine whether the
potential **inhibitor** is active on, e.g., **inhibits**
expression of, at least one of the
allelic forms, but not all of those forms. If the potential
inhibitor inhibits only a
subset of the allefic forms of the particular essential gene, then it is
an allele
specific **inhibitor**. Preferably the difference in activity of
the **inhibitor** for
different allelic forms is between allelic forms which have a sequence
variance at a
particular site.

In many, or even most, cases an allele specific **inhibitor**
discriminates between two
allelic forms due to a particular single sequence variance between the
allelic forms
of the target gene. For example,. . . not affect the cleavage. In the
Detailed Description of the
Invention specific examples of proteins, small molecules, and
oligonucleotides
providing allele specific **inhibition** based on single sequence
variances are
described. Thus, in preferred embodiments an allele specific
inhibitor
discriminates between two allelic forms by discriminating a single
sequence
variance. As previously indicated, **inhibitors** can be targeted
to either the nucleic
acid or a polypeptide (where a nucleotide change results in an amino
acid change).

In particular embodiments, the allele specific **inhibitor** will
recognize more than
one linked sequence variances within a specific allele.

An allele specific **inhibitor** or variance specific
inhibitor is a drug or **inhibitor**
that **inhibits** the activity of one alternative allele of a gene
to a greater degree than
at least one other alternative allele. The difference in activity is
commonly
determined by the dose or level of a drug required to achieve a
quantitative degree
232/116
of **inhibition**. A commonly used measure of activity is the IC50
or concentration
of the drug required to achieve a 50% reduction in the measured activity
of the
target gene. Preferably an allele specific **inhibitor** will have
at least twice the
activity on the target allelic form than on a non-target allelic form,
more
preferably at least. . . most preferably at least 100 times. This can
also
be expressed as the sensitivities of the different allelic forms to the
inhibitor.

. . .
it is equivalent to state that the target allelic form is most
preferably at least 100 times as sensitive to the **inhibitor** as
a non-target allelic
form. The activity of an **inhibitor** can be measured either in
vitro or in vivo, in

assay systems that reconstitute the in vivo system, or in systems incorporating
selected elements of the complete biological system. For use in **inhibiting** cells
containing only the target allelic form rather than cells containing at least one non-
targeted allelic form, the difference in activity. . .

In a related aspect, the invention provides **inhibitors**
potentially useful for tumor,
e.g. . cancer treatment, or treatment of other proliferative disorders. Such
inhibitors are active on a specific allele of a gene which has
at least two different
alleles encoding an essential gene product in one of the target gene categories
above. Such **inhibitors** can, for example, be identified by the
above screemng
methods.

In a related aspect, the invention provides methods for producing
inhibitors active
on such specific allelic forms of belonging to one of the above
categories genes by
232/116
identifying a gene encoding an essential. . . product which has alternative allelic
forms in a non-tumor cell and which undergoes LOH in a tumor cell, screening to
identify an **inhibitor** which is active on at least one but less
than all of the alleles
of the gene, and synthesizing the **inhibitor** in an amount
sufficient to produce a
therapeutic effect when administered to a patient suffering from a tumor in which
tumor cells have only the allele on which the **inhibitor** is
active.

In the context of this invention, the term active on an allefic form or allele
specific **inhibitor** or specific for an allelic form indicates
that the relevant
inhibitor inhibits an allele having a particular
sequence to a greater extent
(preferably > 2x) than an allele having a sequence which differs in a particular
manner. Thus, for alleles for which a particular base position is identified, the
inhibitor has a higher degree of **inhibition** when a
certain base is in the specified
position then when at least one different base is in that position. This. . . means that
for substitution at a particular base position, at least two of the possible allelic
forms differ in sensitivity to an **inhibitor**. Usually, however,
for a specific
sequence variance site, the site will be occupied by one of only two bases.

Further, if an **inhibitor** acts at the polypeptide level, and
any of three bases may be
present at a particular position in a coding sequence but only one of the

substitutions results in an amino acid change, then the activity of the **inhibitor** would be expected to be the same for the two forms producing the same amino acid sequence but different for the form. . .

The term less active indicates that the **inhibitor** will **inhibit** growth of or kill a cell containing only the allelic form of a gene on which the **inhibitor** is more active at concentrations at which it does not significantly **inhibit** the growth of or kill a cell containing only an allelic form on which the **inhibitor** is less active.

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The term drug or **inhibitor** refers to a compound or molecule which, when brought into contact with a gene, its RNA transcript, or its gene product which the compound **inhibits**, reduces the rate of a cellular process, reduces the level of a cellular constituent, or reduces the level of activity of. . . the term to those skilled in the art and not limiting. Thus, the term generally indicates that a compound has an **inhibitory** effect on a cell or process, as understood by those skilled in the art. Examples of **inhibitory** effects are a reduction in expression of a gene product, reduction in the rate of catalytic activity of an enzyme, and reduction. . . formation or the amount of an essential cellular component. The blocking or reduction need not be complete, in most cases, for the **inhibitor** to have useful activity. Thus, in the present invention, **inhibitors** are targeted to genes, their RNA transcript, or their protein product that are essential for cell viability or proliferation. Such **inhibitors** would have the effect of **inhibiting** essential functions, leading to loss of cell viability or **inhibition** of cell proliferation. In preferred embodiments, such **inhibitors** cause cell death or stop cell proliferation. In preferred embodiments of this invention, **inhibitors** specifically include a molecule or compound capable of **inhibiting** one or more, but not all, alleles of genes, their RNA transcript, or their protein product that are essential for cell survival or proliferation. The terms **inhibitor** of a gene or **inhibitor** of an allele as used herein include **inhibitors** acting on the level of the gene, its gene product, its RNA transcript, its protein product, or modifications thereof and is explicitly not limited to those **inhibitors** or drugs that work on the gene sequence itself.

Several types of **inhibitors** are generally recognized in the art. A competitive **inhibitor** is one that binds to the same site on the gene, its

RNA transcript or gene
product as a natural substrate. . . is required for the action of the gene
or gene product, and competitively prevents the binding of that substrate. An
232/116
66 allosteric **inhibitor** is one that binds to a gene or gene product and alters the
activity of the gene or gene product without preventing binding of a substrate or
cofactor. **Inhibition** can also involve reducing the amount of the gene, RNA
transcript, or its protein product, and thus the total amount of activity from the
gene in the cell. Such **inhibition** can occur by action at any of a large number of
different process points, including for example by **inhibiting** transcription or
translation, or by inducing the elimination of the gene, its RNA transcript, or its
protein product where elimination may involve. . . of the target or egress or export from the compartment in which it is active and the process of
excretion or export. **Inhibition** can also be achieved by modifying the structure of
the target, interfering with secondary modifications, or interfering with cofactors
or other ancillary components which are required for its activity. **Inhibitors** can be
comprised of small molecules or polymeric organic compounds including oligopeptides or oligonucleotides.

The term active on a gene or targeted to a gene indicates that an **inhibitor**
exerts its **inhibitory** effect in a manner which is preferentially linked with the
characteristic properties of a gene, its RNA transcript or its gene. . . RNA with other cellular constituents (RNA, protein, cofactors, substrates, etc.)
required for activity. Thus, in general these terms indicate that the **inhibitor** acts
on the gene, its RNA transcript, its protein product, its gene product, or
modifications thereof, or on a reaction or reaction. . .

. . .
from one of the
above categories has undergone loss of heterozygosity. The method involves
administering a therapeutic amount of an allele specific **inhibitor** of such an
essential gene to a patient whose normal somatic cells are heterozygous for that
gene but whose tumor cells contain only a single allelic form of the gene. The
inhibitor is active on the specific allele of the gene present in the tumor cells.

. . .
cancer. The method involves administering to a patient having a precancerous condition or an early stage cancer or cancers an allele specific
inhibitor targeted to an allele of an essential gene for which the normal somatic
cells of the patient are heterozygous and which. . . the

precancerous condition are not clonal from a single cell, the method involves
subsequently administering to the patient a second allele specific **inhibitor** in an
amount sufficient to **inhibit** and preferably kill cells with LOH in which an allele
not targeted by the first **inhibitor** is the only remaining allele of the gene. In most
cases, the second allele specific **inhibitor** will target the alternative allele of the
gene targeted by the first **inhibitor**. However, the second **inhibitor** can also target
an allele of a second essential gene which has undergone LOH. The second gene
may have undergone LOH in. . . affected the first gene due to their proximity on a chromosome, though this is not essential. Additionally, in
other cases, allele specific **inhibition** of one of the alleles of each of 3, 4, or even
232/116
more target genes can be utilized in a serial. . . genes need not be tightly linked so that LOH of the various genes does not necessarily occur
together. By using the serial **inhibition** of an allele of each of the target genes, it
is possible to **inhibit** and preferably kill the full population of precancerous cells in
which LOH has occurred. Thus, the net effect is essentially the same as if allele
specific **inhibitors** of each of the two alternative alleles of one essential gene had
been used.

In the context of the administration of multiple allele specific **inhibitors**, the terms
serial or subsequently indicates that the administration of two or more **inhibitors** is sufficiently temporally separated so that normal somatic cells remain
functional and are therefore able to survive and/or proliferate. Those skilled. . . that the required time will depend on various factors, such
as clearance rate, type and extent of the effect of an **inhibitor** on normal cells, and
additive cellular toxicity, and that appropriate timing can be routinely determined
for particular selections of compounds.

In another related aspect, the invention provides a method for identifying a
potential patient for treatment with an **inhibitor** active on a specific allele of an
essential gene from one of the above categories. The method involves identifying
a patient having. . . the neoplastic cells
contain only a single allele of the gene, then the patient is a potential patient for
treatment with the **inhibitor**.

With respect to identifying patients with precancerous or oligoclonal proliferative
232/116
diseases characterized by LOH, and selecting appropriate allele or variance-

specific **inhibitors** for such patients, in some cases it may not be practical to obtain samples of all proliferative lesions for LOH assays... . . aorta cannot routinely be sampled by biopsy, and dysplastic lesions in the cervix, colon, or bronchus can be multifocal. Therefore, allele specific **inhibitors** can be selected for such conditions based on previously established patterns of LOH for the condition, and on specific testing for. . . . most preferably 100%. However, it is not necessary that 100% of lesions show LOH for a successful treatment by allele specific **inhibitors** because 2,3,4, or even more **inhibitors** can be used in a combined approach to target an ever higher fraction of lesions, and because substantial therapeutic benefit may be achieved by **inhibiting** the proliferation of less than 100% of lesions.

In another aspect, the invention provides a method for identifying a potential patient undergoing transplantation for treatment with an **inhibitor** active on a specific allele of an essential gene from one of the above categories. The method involves identifying a patient undergoing. . . . related aspect, the invention provides a method for treating graft versus host disease in allogenic transplantation in which an allele specific **inhibitor** is used to **inhibit** proliferation of donor cells, e.g. . to **inhibit** stimulation of the donor immune system. In preferred embodiments, the allele specific **inhibitor** is selected by identifying alternative variances or allelic forms of an essential gene that are present in the donor tissues but not the recipient. Therapy with a variance or allele specific **inhibitor** or **inhibitors** that recognizes both alleles of the essential gene that are present in the donor, but not both alleles of the same. . . . another aspect, the invention provides a method for enhancing engraftment of an allogenic bone marrow transplant in which an allele specific **inhibitor** is used to kill or suppress the patient's own bone marrow, providing space for engraftment of the donor cells within the marrow cavity. In preferred embodiments, the allele specific **inhibitor** is selected by identifying alternative forms of an essential gene that are present in the recipient but not the donor marrow. Therapy with an allele specific (generally a variance specific) **inhibitor** that recognizes both forms of the essential gene that are present in the recipient, but not both forms of the same gene. . .

Allele specific **inhibitors** can be used to treat or prevent chimerism by selectively

killing or suppressing proliferation of the patient's own cells without toxicity. . .

. . .

aspect, the invention provides a method for treating cancer in a patient receiving allogenic or autologous transplantation in which an allele specific **inhibitor** is used to kill or **inhibit** the growth of cancer cells without toxicity to the transplanted marrow. In one embodiment, in an autologous, transplantation the allele specific **inhibitor** is selected to recognize one alternative allele of an essential gene remaining in the cancer cell due to LOH in patients. . . therapy of cancer without suppression of the transplanted marrow. In an alternative embodiment, in an allogenic transplantation, therapy with an allele specific **inhibitor** that recognizes the one form of the essential gene that is present in cancer cells due to LOH in the recipient,. . . tissue for selective reimplantation. The present invention provides for an improved method for purging bone marrow of malignant cells using allele specific **inhibitors** of essential genes. The method involves identifying an essential gene with only one variant form remaining in the cancer cells due. . . The patient's bone marrow is then cultivated ex vivo using methods known in the art in the presence of an allele specific **inhibitor** that **inhibits** the allele that is present in the cancer cells, but not the alternative allele that is present in the heterozygous normal bone. . .

In another aspect, the invention provides a method for **inhibiting** growth of or killing a cell containing only one allelic form of a gene by contacting the cell with an **inhibitor** active on that allelic form. The gene has at least two sequence variants in a population, and belongs to one of the categories of essential genes described below. The **inhibitor** is less active on at least one other allelic form of the gene.

In preferred embodiments of the above aspects in which an allele specific **inhibitor** is used to **inhibit** a cell or to treat a patient, a plurality of different **inhibitors** may be used. Preferably different **inhibitors** target a plurality of different variances in a single target gene, or target variances in different target genes, or both. In particular embodiments a plurality of **inhibitors** is used simultaneously, in others there is serial administration using different **inhibitors** or different sets of **inhibitors** in separate administrations, which may be performed as a single set of administrations in which each set of **inhibitors** is administered once, or in multiple serial administrations in which each set of **inhibitors** is

administered more than
once. Such use of multiple **inhibitors** provides enhanced
inhibition, which
preferably includes killing, of the targeted cells. In addition, allele
specific
inhibitors as described can be used in conjunction with other
treatments for
diseases and conditions, including in conjunction with other
chemotherapeutic
agents such. . .

232/116
In a related aspect, an allele specific **inhibitor** can be used
in conjunction with a
conventional antiproliferative or chemotherapeutic agent or therapy,
such therapies
including radiation, immunotherapy, or surgery. In. . .
. . .
with the above aspects, in a further aspect the invention provides a
pharmaceutical composition which includes at least one allele specific
inhibitor.

In preferred embodiments the composition includes at least one allele
specific
inhibitor and a pharmaceutically acceptable carrier. Such
carriers are known in
the art and some commonly used carriers are described in the Detailed
Description
below. Also in preferred embodiments the composition includes two,
three, or
more allele specific **inhibitors**, and may also include a
pharmaceutically acceptable
carrier. In other preferred embodiments, the composition includes at
least one
allele specific **inhibitor** and another antineoplastic agent,
which need not be an
allele specific **inhibitor**. The embodiments of this aspect may
also optionally
include diluents and /or other components as are commonly used in
pharmaceutical compositions or formulations. In embodiments having a
plurality
of allele specific **inhibitors**, the **inhibitors** may
target a plurality of different
variances of a single target essential gene, or may target sequence
variances of a
plurality of. . .

232/116
In accord with the use of pharmaceutical compositions, the present
invention also
provides a packaged pharmaceutical composition comprising an allele
specific
inhibitor as described above, bearing a Food and Drug
Administration use
indication for administration to a patient suffering from a cancer or.
. .

Thus, similar to the above, the invention provides a method for
identifying an
inhibitor potentially useful for treatment of cancer or other
proliferative disorder.

The **inhibitor** is active on a conditionally essential gene, and

the gene is subject to loss of heterozygosity in a cancer. The method. . . least two alleles of a said gene which differ at at least one sequence variance site and testing a potential allele specific **inhibitor** to determine whether the potential **inhibitor** is active on at least one but less than all of the identified alleles. If the potential **inhibitor inhibits** expression of at least one but less than all of the alleles or reduces the level of activity of a product of at least one but less than all of the alleles, this indicates that the potential allele specific **inhibitor** is, in fact such an allele-specific **inhibitor inhibitor**.

Similar to other types of target genes described above, the invention provides **inhibitors**, methods for producing **inhibitors**, pharmaceutical compositions, methods for identifying potential patients, probes, and primers which target or recognize alleles of a conditionally essential gene or utilize **inhibitors** which target such genes.

. . .

also provides methods for preventing the development of cancer, methods for treating a patient suffering from a cancer, and methods for **inhibiting** growth of a cells as described above except that the targeted cells are subjected to an altered condition such that the gene. . .

232/116

In still another aspect, not requiring the use of allele specific **inhibitors**, but still utilizing information about sequence variance or allelic differences between normal somatic cells and cancer cells in a patient, the invention. . .

. . .

above aspects, a conventional therapy acts on a protein or other molecular target in the same pathway as the allele specific **inhibitor**. As an example, the antineoplastic drug hydroxyurea, which **inhibits** ribonucleotide reductase (RR), can be used in conjunction with an allele specific **inhibitor** of RR subunit MI or M2 or another gene that encodes a product important in nucleotide synthesis. Similarly, the antiproliferative drug methotrexate **inhibits** the enzyme dihydrofolate reductase (DHFR), and can be used with allele specific **inhibitors** of DHFR that would result in a differential methotrexate effect on cancer tissues compared to normal proliferating tissues. Alternatively, methotrexate can be used with allele specific **inhibitors** of other genes important in folate metabolism to achieve an enhanced cancer cell specificity for methotrexate. Similarly, the anticancer drug 5-fluorouracil and related compounds can be administered together with an allele specific **inhibitor** of thymidylate synthase (TS)

in a patient
heterozygous for TS and with LOH at the TS gene in proliferating cells, e.g., cancer
cells. Alternatively, an allele specific **inhibitor** of 5-FU degradation or metabolism
can be administered with 5-FU. For example, the enzyme dihydropyrimidine dehydrogenase, which catalyzes the first and rate. . .
. . .
LOH in one or more tumors or other
proliferative disorders. Genes having these characteristics can then be used for
identifying allele specific **inhibitors** and evaluated for use in the other methods of
this invention. Such procedures are routine, as is shown by the Detailed Description. . .

In preferred embodiments of the above methods and **inhibitors** involving particular
target genes or classes or categories of genes, the **inhibitor** or potential **inhibitor** is
a ribozyme which is designed to specifically cleave a particular target allelic form
of a gene (i.e., a nucleotide sequence such. . .

Similarly, in preferred embodiments the **inhibitor** or potential **inhibitor** is an
oligonucleotide, e.g, an antisense oligonucleotide, preferably at least partially an
oligodeoxyribonucleotide. The antisense oligonucleotide is complementary to a
sequence which includes. . .

Thus, derivatives of nucleic acid **inhibitors** include modified nucleic acid
molecules which may contain one or more of: one or more nucleotide analogs,
including modifications in the sugar. . .

Similarly, in preferred embodiments the **inhibitor** or potential **inhibitor** is an
antibody, preferably a monoclonal antibody, which may be complexed or conjugated with one or more other components, or a fragment. . .

An **inhibitor** may also be an oligopeptide or oligopeptide derivative. Such
peptides may be natural or synthetic amino acid sequences, and may have modifications. . .

In other embodiments, the **inhibitor** is a small molecule, for example, a molecule
of one of the structural types used for conventional anticancer chemotherapy.
. . .
region
undergoes LOH at frequencies similar to the marker. Such gene identification
thus further identifies particular cancers which can potentially be treated with
inhibitors targeting sequence variances in those essential genes.
. . .
LOH for other such disorders and cancers, and can further readily
identify essential genes which are potential targets for variance

specific **inhibition**
and the treatment of the corresponding condition and in other aspects of this
invention.

. . .
72 hours after transfection with antisense oligonucleotides. Anti-ras is an oligonucleotide known to have antiproliferative effects against T24 cells. This
oligonucleotide exhibits **inhibition** comparable to the
anti-RPA70 oligonucleotide.

. . .
is two graphs showing that the proliferation of two cell lines homozygous
for different variant forms of the RPA70 gene is **inhibited** to a greater degree by
matched oligonucleotides than by oligorners having a single base mismatch. Cell
proliferation was measured by BrdU incorporation. . .

232/116
Fig. 13 is a graph showing **Inhibition** of BrdU incorporation in A549 cells by
antisense oligonucleotides against the RPA 70 gene. Cells were transfected, as
described previously, with a. . .

Fig. 20 is a graph showing **inhibition** of mutant ras using antisense
oligonucleotides specific for the mutant form, based on information available in
Schwab et al., 1994, PNAS 91:10460. . .

. . .
and
the variant sequences within these genes, have utility for the therapy of cancer and
other disorders through the discovery of variance-specific
inhibitors.

Gene targets for a variance-specific **inhibition** strategy in this invention satisfy three
criteria.

A large number of references have identified essential genes which constitute actual
or potential targets for allele specific **inhibition**. The identification of essential genes
can be approached in various ways.

. . .
carbohydrates, lipids, organic ions, and inorganic ions, or cytoskeletal elements. The loss of homeostasis often results in cell death or apoptosis or
inhibition of cell proliferation. Homeostasis in a living cell is dynamic, and
programed changes in homeostasis are required through the life cycle. .

. . .
those genes whose products are required for maintaining
this homeostasis conducive to cell growth and survival are targets for anti-neoplastic
e.g., anti-cancer, **inhibitors** as described in the methods herein. For example, many
genes are involved in synthetic functions, allowing the cells to produce essential

cellular. . .

. . .

affecting the gene in a neoplastic disorder, establishes that the gene is a target gene potentially useful for identifying allele specific **inhibitors** and for other aspects of the invention. In addition, as described, target genes are useftil in embodiments of certain aspects of the. . .

. . .

(Type I Beta) L25441
GGTI3 (Geranylgeranyltransferase) Y08201
Geranylgeranyltransferase (Type 11 Beta-Subunit) X98001
3.5 Genes required for regulation of levels of organic ions
Gdp Dissociation **Inhibitors**
GDI Alpha (RAB GDP Dissociation **Inhibitor** Alpha) D45021
Rab Gdp (RAB GDP Dissociation **Inhibitor** Alpha) D13988
4) Genes Required to Maintain Cellular Proteins at Levels Compatible with Cell Growth or Survival
Polypeptide precursor biosynthesis
Amino acid biosynthesis and. . . processing peptidase alpha subunit) D50913
MMP7 X07819
Proteasorne Beta 6 D29012
Proteasome Beta 7 D38048
Proteasorne C13 U 1 7496
232/116
Proteasome C2 D00759
Proteasome C7-1 D26599
Proteasome **inhibitor** hPI31 subunit D88378
Proteasome P I 12 D44466
Proteasome P27 ABOO3177
Proteasome P55 ABOO3103
Ubiquitin System
Enzyme E2-17 Kd(Cyclin-selective ubiquitin carrier protein) U73379
ISOT-3(Ubiquitin carboxyl-terminal hydrolase. . .

. . .

Cell Shape and Motility at Levels
Compatible with Cell Growth or Survival
Cell structure genes (Cytoskeleton)
Actin X04098
Beta-Centractin X82207
Capping Protein Alpha U03851
CFL I (**Cofilin**, Non-Muscle Isoform) X95404
Desmin J03191
Dystrophin U26743
Gelsolin X04412
hOGG I (Myosin Light Chain Kinase) ABOO0410
IC Heavy Chain U31089
Itga2 (Integrin, Alpha 2 (CD49B, alpha. . .

Therapy with **inhibitors** of conditionally essential genes involves administration of the **inhibitor** together with a chemical or physical elements that causes the target gene to be essential for cell survival or proliferation. The use of allele specific **inhibitors** in the current invention allows specific killing of cancer cells with such chemical or physical agent since the gene function that is essential for the survival of cells (in the presence of the chemical or physical agent) is **inhibited** in the cancer cell but not in the normal cell.

. . .
are
responsible for maintaining cell survival or proliferation in the presence of a drug or
biological material. For example, a drug that **inhibits** one pathway for maintaining
the level of a cellular constituent within levels required for cell survival or
proliferation may make alternative pathways essential. In a specific embodiment,
the **inhibition** of a synthetic pathway for a cellular constituent may make alternative
synthetic pathways essential for cell survival or proliferation. Alternatively, a. . . from the cell essential for continued survival or
proliferation. It will be evident to those skilled in the art that anything which
inhibits the ability of a cell to survive in the presence of a specific drug that is
designed to be cytostatic or cytotoxic, will sensitize that cell to the effects of the
drug. A chemosensitizing agent is one that **inhibits** a function in the cell that is
conditionally essential due to the administration of a chemotherapeutic drug.

. . .
in DNA repair may be essential that are not essential in the absence of the
external physical force. An agent that **inhibits** functions in the cell that are essential
due to the adminitration of ionizing radition would be termed a radiosensitizing
agent.

. . .
physical factors, determining whether
such genes are subject to loss of heterozygosity, identifying alternative alleles in
these genes and developing allele specific **inhibitors** of alternative forins of the gene.

The administration of such an **inhibitor** to a patient who has two alternative forms of
the gene in normal cells but only one in the cancer cell. . .

Thiopurinemethyltransferase (GenBankU12387)
e. Inactivation or transformation of other drugs including, but not limited to, purine analogs, folate analogs, topoisomerase **inhibitors**
and tubulin acting drugs via specific enzymatic modification.

I-kappa B alpha (GenBank M69043)
Increased expression of exogenous I kappa B-alpha, an **inhibitor** of
NF-kappa B, increases cell sensitivity to ionizing radiation. Thus is conditionally essential for cells exposed to ionizing radiation.

. . .
affect the gene sequence, RNA
sequence, or protein sequence of the gene or its gene products, which would
facilitate the design of **inhibitors** of the protein product, or be a base difference
anywhere within the genomic DNA sequence, including the promoter or intron

regions. Such DNA sequence variance can be exploited to design **inhibitors** of transcription or translation which distinguish between two allefic forms of the targeted gene. Sequence variants that do not alter protein sequence. . .

. . . genes located in regions which are characteristically associated with LOH for a particular cancer, or other tumor are particularly advantageous targets for **inhibitors** useful for treatment of that cancer or tumor because such genes will also characteristically undergo LOH at high frequency. The fact that. . . LOH occurs before the clonal expansion of cancers in precancerous, abnormally proliferating tissue is potentially useful for preventing cancer with allele specific **inhibitors** of essential genes.

. . . disorder will indicate that the allele specific treatment would be appropriate for the disorder. For the application of the general allele specific **inhibition** strategy to such conditions (e.g.. selection of target gene and variance, identification of **inhibitors**, selection of composition and administration method appropriate for the condition and the **inhibitor**), the cells associated with the condition correspond with the tumor, e.g., cancer cells, for the 232/116 methods described in the Summary above.

. . . at least one marker. This does not necessarily represent the maximum fraction of plaques which could potentially be treated with allele specific **inhibitors** because the study did not attempt to determine the sites of maximum LOH on each arm. LOH which is partial arm. . .

. . . allele of the essential gene is lost from the patient's cancer cells, the retained allele can be targeted with an allele specific **inhibitor**. Such an **inhibitor** will kill, or reduce or prevent the growth of cancer cells by abolishing the fimction of an essential gene. Normal cells, which retain both uninhibited and **inhibited** alleles, will survive or grow due to the expression of the uninhibited allele. This is clearly indicated because tumor cells having only one allelic form (after LOH) thrive, thus, normal cells will also function normally with one of two allelic forms **inhibited**.

. . . neuroectodermal tumor
Rhabdomyosarcoma
17q Breast carcinoma
Neurofibroma: N171
22q Acoustic neurinoma
1 8 Renal cell carcinoma Colorectal carcinoma

18q Breast carcinoma Ependymoma
Colorectal carcinoma Meningioma
Neurofibroma
V. Use of variance-specific **inhibitors** of essential genes to treat non-malignant,
proliferative conditions.

. . .

will differ, with, for example, allele A of a hypothetical essential gene lost in some plaques and allele A' in others. An **inhibitor** of allele A would be expected to kill (or arrest growth of) only about half of all the plaques with allele. . . plaques hernizygous for A. To kill the other half of the plaques with allele loss at the target locus would require an **inhibitor** of A'. Simultaneous use of **inhibitors** of A and A' would be highly toxic to diploid normal cells. However serial use of an **inhibitor** directed to allele A followed by an **inhibitor** directed to A' (perhaps repeating treatment for several cycles, or even indefinitely) would alternately abolish essential gene function in one half of all haploid plaque cells and then the other half, leading eventually to death or sustained **inhibition** of proliferation of all plaque cells. Normal cells would retain
232/116
50% gene function in the presence of **inhibitor** (either from allele A or allele A'). This therapeutic approach is applicable to the eradication of any clonal proliferation of cells in. . .

. . .

surgically removed, LOH has been well described. As with atherosclerotic plaques, these tumors are frequently multifocal and therefore the approach of serial **inhibition** of allele A followed by **inhibition** of allele A' would alternately abolish essential gene function in one half of all haploid tumor cells and then the other half, leading eventually to death or sustained **inhibition** of proliferation of all tumor cells.

. . .

one allelic form in individuals whose normal somatic cells are heterozygous for the particular essential gene. The essential gene can therefore be **inhibited** by an allele specific **inhibitor**, i.e., a variance specific **inhibitor**. In some conditions, however, multiple, independently arising lesions in an individual are subjected to LOH in a disease or condition, e.g., in. . .

It was determined that such conditions can be treated using allele specific **inhibitors** despite the presence of both alleles in cells related to the condition.

There are two strategies for such therapy. The first is to serially administer different **inhibitors** targeted to the different allelic forms of the target gene. This

can be accomplished by using **inhibitors** which target the alternative sequence variants of one sequence variance site. Simultaneous administration of **inhibitors** of both allefic forms of an essential gene would **inhibit** the cells which have undergone LOH at that gene, but would also **inhibit** the normal heterozygous cells of the individual. This treatment would **inhibit** essential ftinctions in normal cells as well as cancer cells and have no advantage over the administration of conventional antiproliferative drugs, many of which are **inhibitors** of known essential functions. In contrast, administration of the first **inhibitor** targets the subset of cells which have only the first allelic form of an essential gene. As described for the general strategy, this **inhibitor** will not significantly affect the growth or survival of the normal heterozygous somatic cells. This first administration is followed by administration of a second **inhibitor;** the second

232/116

inhibitor targets the cells which contain only the second allelic form of the gene, and again does not significantly affect the normal. . . will be useful. Similarly, recurring, or even indefinitely continued alternating administrations will provide useful treatment. Likewise, these methods can incorporate the use of **inhibitors** targeted to specific alleles of a plurality, e.g., 2, 3, 4, or more different target genes.

. . .

in non-malignant diseases are not clonal, there may be systematic loss of one parental chromosome allowing effective therapy with only one variance-specific **inhibitor.** This would occur, for example, if there were an inherited or early embryonic mutation within a tumor suppressor gene on one parental. . . of the corresponding normal tumor suppressor gene on the other parental chromosome would lead to abnormal proliferation. In such cases a variance-specific **inhibitor** of an essential gene that was closely linked to the normal tumor suppressor gene would preferentially kill cells in the proliferating lesion.

VI. Characteristics of allele-specific **inhibitors**

As indicated above allele specific **inhibitors** or allele specific anti-neoplastic agents represent a new approach to tumor therapy because they are lethal or significantly **inhibit** the growth only of tumor cells. The advantages of this approach include, first, lack of toxicity to the normal cells of. . . a therapeutic index greater than that of conventional tumor, e.g., cancer chemotherapy drugs, and second, it is not necessary that the **inhibitors** be targeted specifically to the tumor cells, as they can be administered

systemically. As also
described above, usually an allele specific **inhibitor** is
specific for a single
232/116
sequence variance of an essential gene, though in some cases the
inhibitor utilizes
the joint effects of two or more sequence variances on a particular
allele.

It is not necessary for the allele specific **inhibitor** to have
absolute specificity.

. . .
of a gene product
encoded by the essential gene will often show a reduction in gene
activity when
they take up the **inhibitors** of this invention, but should
remain viable due to the
activity of the protein encoded by the uninhibited allele. On the other
hand,
tumor cells expressing only one allele due to LOH, will respond to the
inhibitors
of this invention which are specifically directed to the remaining
allele, with a
greater reduction in gene activity. Growth of tumor cells exposed to the
inhibitors of this invention will be **inhibited** due
to the suppression of either the
synthesis or the biological activity of the essential gene product.

. . .
only two allelic forms in any given individual, the
gene can have more than two allelic forms in a human population.
Accordingly,
inhibitors can be targeted to any of the alleles in the
population. A particular
inhibitor will generally be targeted to a subset of the
allelic forms; the members
of the subset will have a particular sequence variance which provides
the specific
targeting. In some cases, however, the **inhibitor** will jointly
target two, or
possibly more sequence variances.

Once two or more alleles are identified for a target essential gene,
inhibitors of
high specificity for an allele can be designed or identified
empirically. **Inhibitors**
that can be used in the present invention will depend on whether allelic
variation
at a target locus affects the amino acid. . . the mRNA sequence, or
the
DNA in intron and promoter regions. If there is variation at the protein
level,
then classes of **inhibitors** would include low molecular weight
drugs,
oligopeptides and their derivatives, and antibodies, including modified
or partial
232/116
antibody fragments or derivatives. For mRNA or DNA sequence variance the
main class of **inhibitors** are complementary oligonucleotides
and their derivatives
and catalytic RNA molecules such as ribozymes, including modified
ribozymes.

The generation of **inhibitors** of this invention can be

accomplished by a number of
methods. The preferred method for the generation of specific
inhibitors of the
targeted allelic gene product uses computer modeling of both the target
protein
and the specific **inhibitor**. Other methods include screening
compound libraries
or microorganism broths, empirical screening of libraries of peptides
displayed on
bacteriophage, and various immunological approaches.

Further, in the treatment of cancer patients, a therapeutic strategy
includes using
more than one **inhibitor** of this invention to **inhibit**
more than one target. In this
manner, **inhibitors** directed to different proteins essential to
cell growth can be
targeted and **inhibited** simultaneously. The advantage of this
approach is to
increase the specificity of the **inhibition** of proliferation of
cancer cells, while at
the same time maintaining a low incidence of side effects.
. . .
structure of the alternate allelic forms of the proteins, determinants
can be identified which distinguish the allelic forms. Novel low
molecular weight
inhibitors or oligopeptides can then be designed for selective
binding to these
determinants and consequent allele-specific **inhibition**.
Descriptions of targeted
drug design can be found, for example, in I. Kuntz, Structure-Based
Strategies
for Drug Design and Discovery, Science 257:1078-1082. . . have been
described in Piper et
al., Studies Aided by Molecular Graphics of Effects of Structural
Modifications
on the Binding of Antifolate **Inhibitors** to Human Dihydrofolate
Reductase, Proc
Am. Assoc. Cancer Res. Annual Meeting 33:412 (1992); Hibert et al.,
Receptor
3D-Models and Drug Design, Therapie. . .

Low molecular weight **inhibitors** specific for each allelic
protein form can be
predicted by molecular modeling and synthesized by standard organic
chemistry
techniques. Computer modeling can. . .

The **inhibitors** of this invention can be identified by
selecting those compounds
that selectively **inhibit** the growth of cells expressing one
allelic form of a gene,
but do not **inhibit** the activity of the A allelic form.

B. Small Molecule **Inhibitors**
232/116
Low molecular weight **inhibitors** can be identified and
generated by at least one of
the following methods; (1) screening of small organic molecules present
in
microorganism. . .

Inhibition of protein function following differential binding.

Several
mechanisms of **inhibition** are possible including.

competitive **inhibition** of active sites or critical allosteric
sites,
allosteric **inhibition** of protein function,
altering compartmentalization or stability, and
inhibition of quaternary associations.
. . .
compounds that interact with
particular features of a polypeptide or protein or protein complex,
There are clear
precedents for developing drugs, i.e., **inhibitors**, that are
variance-specific
including drugs that are allosteric **inhibitors** of protein
functions. Several lines of
experimental evidence demonstrate that small molecule variance specific
232/116
inhibitors can be designed and constructed for particular
targets. Specifically.

Allosteric (noncompetitive) **inhibition** of protein function may
be induced
by binding ligands to many different surfaces of a protein. Ligands can
cause allosteric **inhibition** by disturbing secondary, tertiary
or quaternary
(subunit-subunit) interactions of a protein. There is ample evidence
that
such effects can e induced by. . .

232/116
Competitive **inhibitors** can exert variance-specific effects by
exhibiting
differential affinities for variant active sites, thereby interfering
with
binding of the substrate or critical allosteric. . .

Competitive **inhibitors** may bind with equal affinity for the
active site but
exerting different effects on the structure or function of the variant
domain.

Allosteric **inhibitors** can exert variance-specific effects by
binding
differentially to variant forms of the active domain and distorting the
structure or function of the. . .
. . .
model the topology and surface chemistry of the target
in detail. These data are useful in optimizing the binding specificity
or
allosteric **inhibitory** function of the product through a series
of iterative
steps once a prototype binding ligand is identified. Structural modeling
of
the target. . .

Sites of allosteric **inhibition**
Most drug development focuses on competitive **inhibitors** of
protein action rather
than noncompetitive, allosteric **inhibitors**. There is no a
priori advantage to a
competitive versus allosteric **inhibitor** except for the fact
that medicinal chemistry

often begins with candidate molecules derived from natural substrates or cofactors. There are, in fact, conceptual advantages to allosteric **inhibitors** since each protein may contain multiple allosteric sites, and allosteric **inhibitors** may be effective at lower concentrations (e.g. those equivalent to the substrate) since there is no need to compete with the substrate. . .

Detailed crystallographic and other structural studies of a variety of enzymes show that the mechanism of allosteric **inhibition** commonly involves conforinational changes (e.g. domain movements) far from the site of contact with the allosteric regulator. These data illustrate the cooperativity. . .

. . .

several well-characterized proteins. Another is to examine the distribution of epitopes for antibodies that bind to the surface of a protein and **inhibit** its function. Analyses of these types show that allosteric sites are widely dispersed within proteins and may comprise the majority of. . .

. . .

Three HIV-1 RT structures have been published, including complexes with double stranded DNA at 3.0 A resolution and with the non-nucleoside **inhibitors** nevirapine (at 3.5A) and -APA (at 2.8A).

Two classes of HIV-1 RT **inhibitors** have been developed. The first class comprises nucleoside analogues including AZT, ddI and ddC. The second class comprises non-nucleoside analogues belonging to. . . 5 shows the location of selected mutations within HIV-1 RT that cause resistance to nucleoside analogues as well as the mechanism of **inhibition** postulated from physical-chemical experiments and structural data; the list is not comprehensive.

Table 4
232/116
Location and postulated mechanism of amino acid substitutions which confer resistance to nucleoside analog **inhibitors**. trp266X - multiple substitutions.

. . .

analog resistance arises from mutations in multiple domains. Many of the mutations are located far from the dNTP binding sites. These changes **inhibit** drug function by altering the conformation of the target protein in a manner analogous to those conformational changes that may be induced by an allosteric **inhibitor**.

232/116
Table 5 summarizes the mutations that alter the function of non-nucleoside **inhibitor** drugs
Table 5
Location and postulated mechanism of amino acid substitutions which

confer
resistance to non-nucleoside analog **inhibitors**.

ala98gly 5b- 6 loop flexibility Pyridinone L-697661,
Nevirapine
leul.00ile 5b- 6 loop -branch Pyridinone L-697661
Nevirapine, TIBO R82913
lyslolglu 5b- 6 loop charge Pyridinone. . . loop flexibility BHAP
U-87201
lys238thr 14 charge BHAP U-87201
trp266X -thumb TIBO R82913
232/116
It is evident from these examples that the substitutions which
inhibit drug functions
are distributed across several domains. Different **inhibitory**
mechanisms have been
postulated in domains throughout the protein, based on the
three-dimensional
structure of the protein. Most involve conforniational disruption of. .
.

Thyrotropin receptor Naturally occurring antibodies against the
thyrotropin
receptor can cause activation of thyroid function (Grave's disease) or
inhibition of
thyroid function (Hashimoto's disease). The sites within the thyrotropin
receptor
that are targeted by these natural antibodies have been mapped in detail
and have
been tested with monoclonal antibodies. Most of the **inhibitory**
antibodies do not
interfere with binding of thyrotropin to its receptor, and thus, are
allosteric rather
than competitive **inhibitors**. Several independent classes of
inhibitory antibodies
have been identified that bind to epitopes within different domains of
the receptor.
. . .
can be deleted by site-directed mutagenesis without disrupting the
function of the receptor. These experiments provide an explicit
precedent for
achieving allosteric **inhibitory** effects from ligands that
target widely dispersed
sequences within the protein.

Thermus aquaticus DNA polymerase The **inhibitory** activity of 24
monoclonal
antibodies to Thermus aquaticus DNA polymerase has been investigated.
The
antibodies recognized 13 non-overlapping epitopes. Antibody binding to
eight
epitopes was **inhibitory**. **Inhibitory** antibodies
mapped to several distinct domains,
including the 5'nuclease domain, the polymerase domain and the boundary
region
between the 5'nuclease and polyinerase domains. Some antibodies
recognized
epitopes overlapping the DNA binding groove of the polymerase.
Significantly, the
inhibitory antibodies recognized epitopes constituting as much
as 50% of the Taq
polymerase surface, and the non-**inhibitory** antibodies a
further -25%.

. . .
the pharmaceutical industry has worked to develop chemically modified penicillins and cephalosporins to elude inactivation by P-lactamases. In addition, a P-lactarnase **inhibitor** (clavulanic acid) has also been introduced into clinical use.

. . .
associated with drug resistance distributed evenly across the 740 amino acids of the protein. The mechanism by which some of these substitutions **inhibit** katG function can be inferred from the structure of the homologous yeast and E. coli enzymes and knowledge of the catalytic. . .

The application of small molecule **inhibitor** identification is specifically discussed in Example 39 below in connection with the methylguanine methyltransferase gene.

C. Antibody **Inhibition**.

Antibody **inhibitors** are most effective when they are directed against cell surface proteins or receptors. If the essential protein produced by the targeted allele is not a cell surface protein or receptor, the development of antibody **inhibitors** may also require the use of a special antibody-delivery system to facilitate entry of the antibody into the tumor cells. The plasma. . . the structure of the variable region of allele specific antibodies can be used as the basis for design of smaller allele specific **inhibitory** molecules.

. . .
receptors or other polypeptides essential for cell viability. Methods for screening peptide sequences which have high specificity for binding to, and functional **inhibition** of, a specific polypeptide target have been well described previously. Scott, J.K. and Smith G.P., Searching for Peptide Ligands with an Epitope. . . by phage display of polypeptide sequences as well as direct screening of peptides or mixtures of synthetic peptides for binding to or **inhibition** of the target Rinctional polypeptide.

. . .
Ribozymes
Oligonucleotides or oligonucleotide analogs which interact with complementary sequences of cellular target DNA or RNA can be synthesized and used to **inhibit** or control gene expression at the levels of transcription or translation. The oligonucleotides of this invention can be either oligodeoxyribonucleotides or oligoribonucleotides, or. . . they can act enzymatically, such as ribozymes. Both antisense RNA and DNA can be used in this capacity as chemotherapeutic agents for **inhibiting** gene transcription or translation. Trojan, J.,

et aL, Treatment and prevention of rat glioblastoma, by immunogenic C6 cells
expressing antisense insulin-like growth. . .

Inhibitory complementary oligonucleotides may be used as **inhibitors** for cancer
therapeutics because of their high specificity and lack of toxicity.

Included in the scope of the invention are oligoribonucleotides, including antisense
RNA and DNA molecules and ribozymes that function to **inhibit** expression of an
essential gene in an allele specific manner. Anti-sense RNA and DNA molecules
act to directly block the translation of. . .

A specific application of generating **inhibitors** which are either complementary
oligonucleotides or **inhibitory** oligopeptides is described in Holzmayer, Pestov, and
Roninson, Isolation of dominant negative mutants and **inhibitory** antisense RNA
sequences by expression selection of random DNA fragments, Nucleic Acids
Research 20:711-717 (1992). In this study, genetic suppressor elements
(GSEs). . .

Preferred oligonucleotide **inhibitors** include oligonucleotide analogues which are
resistant to degradation or hydrolysis by nucleases. These analogues include
neutral, or nonionic, methylphosphonate analogues, which retain. . .

F, Gene Therapy
Nucleic acid molecules encoding oligonucleotide or polypeptide **inhibitors** will also
be useftil in gene therapy (reviewed in Miller, Nature 357:455-460, (1992). Miller
indicates that advances have resulted in practical approaches. . .

A nucleic acid sequence encoding an **inhibitor** may be administered utilizing an ex
vivo approach whereby cells are removed from an animal, transduced with the nucleic acid
sequence and reimplanted. . .

Many nonviral techniques for the delivery of a nucleic acid sequence encoding an
inhibitor into a cell can be used, including direct naked DNA uptake (e.g., Wolff et
al., Science 247: 1465-1468, 1990), receptor-mediated DNA. . .
. . .
its simplest form, gene transfer can be performed by simply injecting minute
amounts of DNA (e.g., a plasmid vector encoding an **inhibitor**) into the nucleus of a
cell, through a process of microinjection. Capecchi MR, Cell 22:479-88 (1980).

232/116
In another preferred embodiment, a vector having nucleic acid sequences encoding
an allele specific **inhibitor** is provided in which the nucleic

acid sequence is
expressed only in specific tissue. Examples or methods of achieving tissue-specific
gene expression. . .

V11. Utility of allele-specific **inhibitors** of essential genes
A, Conditions susceptible to therapy.

The fraction of all cancers could be treated with allele specific **inhibitors** directed
against allele specific essential gene targets is a function of the frequency of the
target allele and the frequency of LOH.. . . exist in two allelic forms, each with an allele
frequency of 0.5 so that half the population would be heterozygous. An **inhibitor** of
one allele of such an ideal target would be a useful agent for 25% of all cancer
patients. An **inhibitor** of the other allele of the same ideal target would be
therapeutic for an additional 25% of all patients, making 50%. . .

Allele specific **inhibitors** of both alleles of such targets would be expected to
address 0.4 x 0.5 = 0.2 or 20% of the relevant. . .

. . .
<------User Break------>

```
=> s actin
         15854 ACTIN
           208 ACTINS
L24      15915 ACTIN
                (ACTIN OR ACTINS)

=> s stabil?
L25     282338 STABIL?

=> s ewing?
L26       3185 EWING?

=> s l26 and l24
L27       1098 L26 AND L24

=> s l27 and l25
L28       1004 L27 AND L25

=> s l24/ab
            151 ACTIN/AB
              1 ACTINS/AB
L29         152 (ACTIN/AB)
                ((ACTIN OR ACTINS)/AB)

=> s l29 and l26
L30           5 L29 AND L26

=> s l30 and l25
L31           5 L30 AND L25

=> d ibib 1-5

L31    ANSWER 1 OF 5     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:       2006029046 PCTFULL  ED 20060403  EW 200611
TITLE (ENGLISH):        USE OF LEPTIN IN WOUND HEALING
```

TITLE (FRENCH): UTILISATION DE LEPTINE DANS LA GUERISON DE PLAIE
INVENTOR(S): SIERRA-HONIGMANN, Maria Rocio, 656 Camino de la Luna, Thousand Oaks, California 91320, US
PATENT ASSIGNEE(S): YALE UNIVERSITY, Office of Cooperative Research, 433 Temple Street, New Haven, Connecticut 06511, US
AGENT: LEVY, Seth, D. et al.$, Suite 2400, 865 South Figueroa Street, Los Angeles, California 90017-2566; 90017-2566$, US
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2006029046	A2	20060316

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
RW (ARIPO): BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LT LU LV MC NL PL PT RO SE SI SK TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2005-US31455 A 20050902
PRIORITY INFO.: US 2004-60607115 20040903

L31 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2005042726 PCTFULL ED 20050519 EW 200519
TITLE (ENGLISH): METHODS FOR MODULATING AN IMMUNE RESPONSE BY MODULATING KRC ACTIVITY
TITLE (FRENCH): METHODES PERMETTANT DE MODULER UNE REPONSE IMMUNITAIRE PAR MODULATION DE L'ACTIVITE DE KRC
INVENTOR(S): GLIMCHER, Laurie, H., 51 Hampshire Street, West Newton, MA 02165, US [US, US];
OUKKA, Mohamed, 46 Englewood Avenue, Brighton, MA 02146, US [US, US]
PATENT ASSIGNEE(S): PRESIDENT AND FELLOWS OF HARVARD COLLEGE, 1350 Massachusetts Avenue, Suite 727, Cambridge, MA 02138, US [US, US], for all designates States except US;
GLIMCHER, Laurie, H., 51 Hampshire Street, West Newton, MA 02165, US [US, US], for US only;
OUKKA, Mohamed, 46 Englewood Avenue, Brighton, MA 02146, US [US, US], for US only
AGENT: DECONTI, Giulio, A.$, Lahive & Cockfield, LLP, 28 State Street, Boston, MA 02109$, US
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2005042726	A2	20050512

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

RW (ARIPO): BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LU MC NL PL PT RO SE SI SK TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2004-US36641 A 20041103
PRIORITY INFO.: US 2003-10/701,401 20031103

L31 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2003027235 PCTFULL ED 20030410 EW 200314
TITLE (ENGLISH): AFAP SEQUENCES, POLYPEPTIDES, ANTIBODIES AND METHODS
TITLE (FRENCH): SEQUENCES AFAP, POLYPEPTIDES, ANTICORPS ET PROCEDES ASSOCIES
INVENTOR(S): FLYNN, Daniel, C., 418 Shawnee Drive, Morgantown, WV 26508-0911, US
PATENT ASSIGNEE(S): WEST VIRGINIA UNIVERSITY RESEARCH CORPORATION, P.O. Box 6216, 201 Chestnut Ridge Research Building, Morgantown, WV 26506-6216, US [US, US]
AGENT: SPAR, Elizabeth, N.$, Palmer & Dodge LLP, 111 Huntington Avenue, Boston, MA 02199-7613$, US
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2003027235	A2	20030403

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2002-US29559 A 20020918
PRIORITY INFO.: US 2001-60/323,866 20010921

L31 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2002102846 PCTFULL ED 20030115 EW 200252
TITLE (ENGLISH): PHARMACEUTICAL COMPOSITION FOR DIAGNOSIS, PREVENTION OR TREATMENT OF A TUMOROUS STATE, COMPRISING A MODULATOR OF THE ACTIN POLYMERISATION STATE
TITLE (FRENCH): COMPOSITION PHARMACEUTIQUE POUR LE DIAGNOSTIC, LA PREVENTION OU LE TRAITEMENT D'UNE PATHOLOGIE TUMORALE, COMPRENANT UN AGENT MODULATEUR DE L'ETAT DE POLYMERISATION DE L'ACTINE
INVENTOR(S): AUCLAIR, Christian, 22, avenue Parmentier, F-75011 Paris, FR [FR, FR];
AMSELLEM, Valerie, 103, avenue Philippe-Auguste, F-75011 Paris, FR [FR, FR];
HERVY, Martial, 5, rue de l'Amiral Mouchez, F-75013 Paris, FR [FR, FR];
SUBRA, Frederic, 3 bis, rue d'Athenes, F-75009 Paris, FR [FR, FR]
PATENT ASSIGNEE(S): BIOALLIANCE PHARMA, 59, rue du General Martial Valin, F-75015 Paris, FR [FR, FR], for all designates States except US;
ECOLE NORMALE SUPERIEURE DE CACHAN, 61, avenue du President Wilson, F-94235 Cachan Cedex, FR [FR, FR],

for all designates States except US;
INSTITUT GUSTAVE ROUSSY-IGR, 39, rue Camille Desmoulins, F-94805 Villejuif Cedex, FR [FR, FR], for all designates States except US;
CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE -CNRS-, 3, rue Michel Ange, F-75794 Paris Cedex 16, FR [FR, FR], for all designates States except US;
AUCLAIR, Christian, 22, avenue Parmentier, F-75011 Paris, FR [FR, FR], for US only;
AMSELLEM, Valerie, 103, avenue Philippe-Auguste, F-75011 Paris, FR [FR, FR], for US only;
HERVY, Martial, 5, rue de l'Amiral Mouchez, F-75013 Paris, FR [FR, FR], for US only;
SUBRA, Frederic, 3 bis, rue d'Athenes, F-75009 Paris, FR [FR, FR], for US only

AGENT: BRESSE, Pierre$, Bresse-Majerowicz, 3, avenue de l'Opera, F-75001 Paris$, FR

LANGUAGE OF FILING: French
LANGUAGE OF PUBL.: French
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002102846	A2	20021227

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-FR2106 A 20020618
PRIORITY INFO.: FR 2001-01/07976 20010618

L31 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999022028 PCTFULL ED 20020515
TITLE (ENGLISH): MODULATORS OF ACTIN
TITLE (FRENCH): MODULATEURS D'ACTINE
INVENTOR(S): KING, Mary-Claire;
LYNCH, Eric, D.;
LEE, Ming, K.;
MORROW, Jan, E.;
WELCSH, Piri, L.;
LEON, Pedro, E.

PATENT ASSIGNEE(S): THE UNIVERSITY OF WASHINGTON;
THE UNIVERSITY OF COSTA RICA

LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9922028	A1	19990506

DESIGNATED STATES
W: CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.: WO 1998-US23024 A 19981029
PRIORITY INFO.: US 1997-60/063,737 19971029
US 1998-09/080,897 19980518

```
=> d kwic 31
      5 ANSWERS ARE AVAILABLE.  SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
The answer numbers requested are not in the answer set.
ENTER ANSWER NUMBER OR RANGE (1):eng
ANSWER NUMBERS NOT CORRECTLY SPECIFIED
Enter an answer number,       Example: 10
several answer numbers,       Example: 3,7,10
a range of answer numbers,    Example: 5-10
or a combination of these.    Example: 3,7,9-10,15
ENTER ANSWER NUMBER OR RANGE (1):end

=> d kwic 3

L31    ANSWER 3 OF 5     PCTFULL   COPYRIGHT 2006 Univentio on STN
ABEN   The present invention comprises reagents and methods which target
       actin filaments or the cellular signals that control
       actin filament integrity. Specifically, the invention provides
       novel actin binding polypeptides (e.g., human AFAP
       polypeptides), antibodies which specifically recognize the same, nucleic
       acids encoding the same, and methods for.  .  .

DETD   .  .  .  aspect, the pathology is cancer, e.g., such as breast cancer,
       colon cancer,
       prostate cancer, lung cancer, a cancer involving neural cells,
       Ewing sarcoma and
       rhabdomyosarcoma.
 .  .  .
       acids comprising one or more of modified bases, sugars, and
       intermicleotide linkages
       which preferably have the substantially the same or enhanced
       stability and/or specificity for a
       target nucleic acid as the nucleic acids from which they are derived.
 .  .  .
       Antisense nucleic acids can also be
       chemically synthesized and can be deoxynucleotides or modified forms
       thereof which are
       selected to have enhanced stability in vivo.
 .  .  .
       activated in a number of human cancers including breast cancer,
       colon cancer, prostate cancer, lung cancer (e.g., small lung cell
       carcinoma), neuroblastoma,
         Ewing sarcoma and rhabdomyosarcoma (Cartwright et al., 1990,
       supra; Rosen et al., 1986,
       supra).
 .  .  .
       breast cancer, colon cancer, prostate cancer, lung cancer
       (e.g., small lung cell carcinoma), a cancer involving neural cells
       (e.g., such as neuroblastoma),
         Ewing sarcoma and rhabdomyosarcoma.
 .  .  .
       forms thereof. In one aspect, the condition is cancer (e.g.,
       such as breast cancer, colon cancer, prostate cancer, lung cancer,
       neuroblastoma, Ewing sarcoma
       and rhabdomyosarcoma). In another aspect, the condition is a
       neurological disease (which can
       47
       The agents, agonists, and antagonists may be formulated.  .  .
 .  .  .
       and coverslips and observed under confocal microscopy (Zeiss,
       Oberkochen, Germany). Samples for negative staining were adsorbed to
       grids coated with
       nitrocellulose and stabilized with carbon (Ernest F. Fullam,
```

Latham, NY). Unbound protein was
removed by successive washes with buffer and water before staining with.
. .

CLMEN. . . said cancer is selected from the group
consisting of. breast cancer, colon cancer, prostate cancer, lung
cancer, a cancer
involving neural cells, **Ewing** sarcoma and rhabdomyosarcoma.

=> d kwic 5

L31 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ABEN The invention provides methods and compositions which find use, i(inter
alia), for modulating
the **stabilization** of **actin** filaments. The
compositions may comprise one or more polypeptide moieties
derived from a novel human diaphanous polypeptide and/or one or. . .
ABFR L'invention concerne des procedes et des compositions permettant, entre
autres choses, de
moduler la **stabilisation** des filaments d'actine. Ces
compositions peuvent comprendre une ou
plusieurs fractions de polypeptide derivees d'un nouveau polypeptide
diaphane de l'homme. . .

DETD INTRODUCTION
Field of the Invention
The invention relates to a class of polypeptides involved in actin
stabilization.
. . .
of the Invention
The actin cytoskeleton plays a central role in defining cellular
structure and effecting
dynamic changes in morphology. By selectively **stabilizing** and
destabilizing actin
polymerization, the cell is able to effect a wide range of structural
reorganization and effect
phenomena such as cell. . .

the progress of many pathogenic infections, invasion and metastisis of
neoplasia, fertilization,
clotting and wound repair, etc., the **stability** of actin
polymerization is a choice target for
therapuetic intervention. In fact, potent drugs effecting actin filament
destabilization and
stabilization such as fungal-derived alkaloids including the
cytochalasins and phalloidins are
well known. Here we disclose a new family of modulators of actin polymer
stabilization
derived from a novel human diaphanous protein and gene.

SUMMARY OF THE INVENTION
The invention provides methods and compositions which find use. inter
alia, for
modulating the **stabilization** of actin filaments. The
compositions may comprise one or more
polypeptide moieties derived from a novel human diaphanous polypeptide
and/or one. . .
. . .
other polypeptide moieties, complexed in a wide variety of
covalent and/or non-covalent associations and binding complexes, etc.,
which may provide
enhanced activity, **stability**, availability, targeting, etc.

. . .
polypeptide
hDial-del-15: CYCLIN B2 - residues 1141-1171 of SEQ ID NO:2 fusion polypeptide
The invention provides methods and compositions of selectively modulating
cytoskeletal de/**stabilization** and/or the effective concentration of a human diaphanous protein
within a target cell. The general methods involve introducing into the target. . . the human diaphanous polypeptide moiety, the modulator may
comprise a wide variety of additional moieties, including moieties which provide for
detection, targeting, **stability**, proteolytic resistance, etc. Preferred modulators demonstrate
cytoskelatal de/**stabilization** with several alternative methods of introduction, including direct
medium uptake, uptake facilitated by chaotropic agents including detergents (e.g. TWEEN20,
etc.), guanadine salts,. . .
. . .
to a probe specific for the binding agent. Agents of particular interest modulate human diaphanous polypeptide function, e.g. human diaphanous
5
polypeptide-dependent actin de/**stabilization**.
. . .
usually RNA or DNA, it is often advantageous to use nucleic acids comprising other bases or nucleotide analogs to provide modified **stability**, etc.
. . .
3.0 were transferred to a UNIX-based Sun workstation for cont-ig' assembly and blast analysis. The computer program PHRED (Green P and **Ewing** B. 1996.
. . .
phrap.docs/ phred.html) was used to assign bases to the electropherograms. After eliminating vector sequences, the program PHRAP (Green P
1 0 and **Ewing** B. 1996. http:H www.bozeman.mbt.washington.edu/ phrap.docs/ phrap.html) was
used to analyze the sequences, identify overlapping individual sequences, and assemble them
into contigs. To. . .
. . .
daily blood and peritoneal sample to evaluate peritoneal fluid cell counts,
hernatological cell counts, serum chemistries, bacterial cultures as needed, vector **stability**,
viral uptake by cells, expression of hDial gene and presence of antibodies to vector envelope
proteins. At four week intervals patients are. . .

Detection of vector **stability** and expression. DNA is prepared from cell samples by
hypotonic lysis, digestion with proteinase K (Boehringer Mannheim, Indianapolis. Indiana)
and SDS, followed. . .

PCR primers specific for the neo sequences within the LXSN-hDialsv vector are
employed for determination of vector presence and **stability** within patient samples. RT-PCR
is performed by our published methods (Thompson, M. E., et al. Nature

```
       Genetics 9, 444-
       450] 1995.).


=> s ewing sarcoma or (ewing? sarcoma
UNMATCHED LEFT PARENTHESIS 'OR (EWING?'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s ewing sarcoma or (ewing? sarcoma)
          3035 EWING
           132 EWINGS
          3112 EWING
                 (EWING OR EWINGS)
         18118 SARCOMA
          5088 SARCOMAS
             5 SARCOMATA
         19804 SARCOMA
                 (SARCOMA OR SARCOMAS OR SARCOMATA)
           392 EWING SARCOMA
                 (EWING(W)SARCOMA)
          3185 EWING?
         18118 SARCOMA
          5088 SARCOMAS
             5 SARCOMATA
         19804 SARCOMA
                 (SARCOMA OR SARCOMAS OR SARCOMATA)
           400 EWING? SARCOMA
                 (EWING?(W)SARCOMA)
L32        400 EWING SARCOMA OR (EWING? SARCOMA)

=> d his

     (FILE 'HOME' ENTERED AT 14:41:45 ON 17 APR 2006)

     FILE 'REGISTRY' ENTERED AT 14:41:55 ON 17 APR 2006
                E "DOLASTATIN"/CN 25
L1            1 S E6

     FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006
L2        52669 S ACTIN
L3          812 S COFILIN
L4      1968300 S ANTAG? OR INHIBIT?
L5          222 S L4 (L) L3
L6         1659 S EWING?
L7            1 S L6 AND L5
L8           22 S L1
L9            0 S L8 AND L6
L10         224 S ZYXIN
L11           3 S L10 AND L6
L12           6 S L3 AND L6
L13           4 S L12 AND L4
L14         989 S PHOSPHOINOSITOL?
L15           0 S L14 AND L6
L16          98 S PHOSPHOTIDYLINOSITOL
L17           0 S L15 AND L6

     FILE 'PCTFULL' ENTERED AT 14:49:15 ON 17 APR 2006
L18         188 S COFILIN
L19        3185 S EWING?
L20          19 S L19 AND L18
L21      198141 S ANTAG? OR INHIBIT?
L22          19 S L20 AND L21
```

```
L23           4 S L22 NOT PY>2001
L24       15915 S ACTIN
L25      282338 S STABIL?
L26        3185 S EWING?
L27        1098 S L26 AND L24
L28        1004 S L27 AND L25
L29         152 S L24/AB
L30           5 S L29 AND L26
L31           5 S L30 AND L25
L32         400 S EWING SARCOMA OR (EWING? SARCOMA)

=> s l32 and l24
L33         165 L32 AND L24

=> s l33 and l25
L34         137 L33 AND L25

=> s l34 not py>2001
        488865 PY>2001
L35          54 L34 NOT PY>2001

=> s l35 and l29
L36           0 L35 AND L29

=> s l24/clm
L37        1198 (ACTIN/CLM)

=> s l37 and l35
L38           5 L37 AND L35

=> s l24/ti
L39          44 (ACTIN/TI)

=> s l39 and l35
L40           0 L39 AND L35

=> d ibib l38 1-5

L38    ANSWER 1 OF 5     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2001055368 PCTFULL  ED 20020827
TITLE (ENGLISH):         NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH):          ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S):             ROSEN, Craig, A.;
                         BARASH, Steven, C.;
                         RUBEN, Steven, M.
PATENT ASSIGNEE(S):      HUMAN GENOME SCIENCES, INC.;
                         ROSEN, Craig, A.;
                         BARASH, Steven, C.;
                         RUBEN, Steven, M.
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 2001055368         A1 20010802
DESIGNATED STATES
       W:                AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
                         CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
                         IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
                         MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
                         TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
                         SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
                         DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
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APPLICATION INFO.:	WO 2001-US1348	A	20010117
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	US 2000-60/254,097 20001211
	US 2001-60/259,678 20010105

L38 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 2001055328 PCTFULL ED 20020827

TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES

TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS

INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.

PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055328	A2	20010802

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US 2000-60/254,097 20001211
US 2001-60/259,678 20010105

L38 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001055201 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER KIND DATE

	WO 2001055201 A1 20010802
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APPLICATION INFO.:	WO 2001-US1317 A 20010117
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US 2001-60/259,678 20010105

L38 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001054733 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001054733	A1	20010802

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APPLICATION INFO.: WO 2001-US1312 A 20010117
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US 2000-60/235,834	20000927
US 2000-60/235,836	20000927
US 2000-60/236,369	20000929
US 2000-60/236,327	20000929
US 2000-60/236,370	20000929
US 2000-60/236,368	20000929
US 2000-60/236,367	20000929
US 2000-60/237,039	20001002
US 2000-60/237,038	20001002
US 2000-60/237,040	20001002
US 2000-60/237,037	20001002
US 2000-60/236,802	20001002

US 2000-60/239,937	20001013
US 2000-60/239,935	20001013
US 2000-60/241,785	20001020
US 2000-60/241,809	20001020
US 2000-60/240,960	20001020
US 2000-60/241,787	20001020
US 2000-60/241,808	20001020
US 2000-60/241,221	20001020
US 2000-60/241,786	20001020
US 2000-60/241,826	20001020
US 2000-60/244,617	20001101
US 2000-60/246,474	20001108
US 2000-60/246,532	20001108
US 2000-60/246,476	20001108
US 2000-60/246,526	20001108
US 2000-60/246,475	20001108
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US 2000-60/246,528	20001108
US 2000-60/246,527	20001108
US 2000-60/246,477	20001108
US 2000-60/246,611	20001108
US 2000-60/246,610	20001108
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US 2000-60/246,609	20001108
US 2000-60/246,478	20001108
US 2000-60/246,524	20001108
US 2000-60/246,523	20001108
US 2000-60/249,299	20001117
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US 2000-60/249,216	20001117
US 2000-60/249,217	20001117
US 2000-60/249,211	20001117
US 2000-60/249,215	20001117
US 2000-60/249,218	20001117
US 2000-60/249,208	20001117
US 2000-60/249,213	20001117
US 2000-60/249,212	20001117
US 2000-60/249,207	20001117
US 2000-60/249,245	20001117
US 2000-60/249,244	20001117
US 2000-60/249,297	20001117
US 2000-60/249,214	20001117
US 2000-60/249,264	20001117
US 2000-60/249,209	20001117
US 2000-60/249,300	20001117
US 2000-60/249,265	20001117
US 2000-60/250,391	20001201
US 2000-60/250,160	20001201
US 2000-60/256,719	20001205
US 2000-60/251,030	20001205
US 2000-60/251,988	20001205
US 2000-60/251,479	20001206
US 2000-60/251,869	20001208
US 2000-60/251,856	20001208
US 2000-60/251,868	20001208
US 2000-60/251,990	20001208
US 2000-60/251,989	20001208
US 2000-60/254,097	20001211
US 2001-60/259,678	20010105

L38 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001053514 PCTFULL ED 20020827
TITLE (ENGLISH): TOXICANT-INDUCED DIFFERENTIAL GENE EXPRESSION

TITLE (FRENCH):	EXPRESSION GENETIQUE DIFFERENTIELLE INDUITE PAR SUBSTANCES TOXIQUES
INVENTOR(S):	REIDHAAR-OLSON, John, F.
PATENT ASSIGNEE(S):	GLAXO GROUP LIMITED; REIDHAAR-OLSON, John, F.
DOCUMENT TYPE:	Patent
PATENT INFORMATION:	

NUMBER	KIND	DATE
WO 2001053514	A1	20010726

DESIGNATED STATES

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:	WO 2001-US1920	A	20010119
PRIORITY INFO.:	US 2000-09/489,220		20000121

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PASSWORD:
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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 8	JAN 30	Saved answer limit increased
NEWS 9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 14	FEB 28	TOXCENTER reloaded with enhancements
NEWS 15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 16	MAR 01	INSPEC reloaded and enhanced
NEWS 17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 18	MAR 08	X.25 communication option no longer available after June 2006
NEWS 19	MAR 22	EMBASE is now updated on a daily basis
NEWS 20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS 22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS 23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS 25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

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NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 16:12:12 ON 17 APR 2006

=> file pctfull
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'PCTFULL' ENTERED AT 16:12:30 ON 17 APR 2006
COPYRIGHT (C) 2006 Univentio

FILE LAST UPDATED:          11 APR 2006      <20060411/UP>
MOST RECENT UPDATE WEEK:        200614        <200614/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
    SEE
    http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE
    (last updated April 10, 2006) <<<

=> s jasplakinolide
           171 JASPLAKINOLIDE
             1 JASPLAKINOLIDES
L1         171 JASPLAKINOLIDE
                 (JASPLAKINOLIDE OR JASPLAKINOLIDES)

=> s ewing? (2W) sarcoma
          3185 EWING?
         18118 SARCOMA
          5088 SARCOMAS
             5 SARCOMATA
         19804 SARCOMA
                 (SARCOMA OR SARCOMAS OR SARCOMATA)
L2        1574 EWING? (2W) SARCOMA

=> s l2 and l1
L3          36 L2 AND L1

=> s l3 not py>2001
        488865 PY>2001
L4           1 L3 NOT PY>2001

=> d ibib

L4     ANSWER 1 OF 1     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:       2000071135 PCTFULL  ED 20020515
TITLE (ENGLISH):        ANTI-TUMOR COMPRISING BOROPROLINE COMPOUNDS
TITLE (FRENCH):         AGENTS ANTI-TUMORALES CONTENANT DES COMPOSES DE
                        BOROPROLINE
INVENTOR(S):            WALLNER, Barbara, P.;
                        MILLER, Glenn
PATENT ASSIGNEE(S):     POINT THERAPEUTICS, INC.
LANGUAGE OF PUBL.:      English
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DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 2000071135	A1	20001130

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ
TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK
ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM
GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US14505 A 20000525
PRIORITY INFO.: US 1999-60/135,861 19990525

=> d kwic

L4 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . myxoid liposarcomas and pleiomorphic
liposarcomas), leiomyosarcomas, rhabdomyosarcomas, malignant peripheral
nerve sheath
tumors (also called malignant schwannomas, neurofibrosarcomas, or
neurogenic sarcomas),
Ewing's tumors (including **Ewing**'s **sarcoma** of bone,
extraskeletal [not bone] **Ewing**'s
io **sarcoma**, and primitive neuroectoderinal tumor [PNET]),
synovial sarcoma, angiosarconias,
hemangiosarcomas, lymphangiosarcomas, Kaposi's sarcoma,
hemangioendothelioma,
fibrosarcoma, desmoid tumor (also called aggressive fibromatosis),
dermatofibrosarcoma
protuberans (DFSP),. . .
. . .
immunostimulant peptides-, insulin-like growth factor-I receptor
inhibitoi, interferon
agonists; interferons; interleukins; iobenguane; lododoxorubicin;
lporneanol, 4-; irinotecan;
iroplact; irsogladine; isobengazole; isohomohalicondrin B; itasetron;
jasplakinolide;
kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin;
lenograstim; lentinan sulfate;
leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha
interferon; leuprolide +
estrogen + progesterone; leuprorelin;. . .

=> s hepatocarcinoma? or mesenchymal or neuroectodermal
463 HEPATOCARCINOMA?
4765 MESENCHYMAL
1 MESENCHYMALS
4765 MESENCHYMAL
(MESENCHYMAL OR MESENCHYMALS)
922 NEUROECTODERMAL
1 NEUROECTODERMALS
922 NEUROECTODERMAL
(NEUROECTODERMAL OR NEUROECTODERMALS)
L5 5608 HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL

=> s l5 and l4

L6 1 L5 AND L4

=> d kwic\
'KWIC\' IS NOT A VALID FORMAT FOR FILE 'PCTFULL'

The following are valid formats:

ALL, MAX--------BIB plus IND plus ABS plus TX
ALLG------------ALL, MAX plus GI
BIB-------------AN, ED, UP, EW, UW, TIEN, TIFR, TIDE, TIES, IN, PA, LA, LAF
DT, PI, DS, AI, PRAI
BIBG------------BIB plus GI
IND, IPC--------ICM, ICS
ABS-------------ABEN, ABF, ABFR, ABDE, ABES
TX--------------DETD, CLM
IALL,IMAX-------ALL indented with text labels
IALLG,IMAXG-----IALL, IMAX plus GI
DALL------------Delimited ALL format
STD-------------BIB plus IND
STDG------------STD plus GI
ISTD------------STD indented with text labels
ISTDG-----------ISTD plus GI
BRIEF-----------BIB plus ABS
BRIEFG----------BIB plus ABS plus GI
IBRIEF----------BRIEF indented with text labels
IBRIEFG---------IBRIEF plus GI
SCAN------------TI (random display without AN)
TRIAL (TRI)-----FA, TI, CLMN, DETN
SAMPLE (SAM)----FA, TI, CLMN, DETN
FREE------------FA, TI, CLMN, DETN
ENTER DISPLAY FORMAT (STD):kwic

L6 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . epithelium eductus semicircularis, enamel epithelium, false epithelium,
germinal epithelium, gingival epithelium, glandular epithelium, glomerular epithelium,
laminated epithelium, epithelium of lens, epithelium lentis, **mesenchymal** epithelium,
olfactory epithelium, pavement epithelium, pigmentary epithelium, pigmented epithelium,
protective epithelium, pseudostratified epithelium, pyramidal epithelium, respiratory
epithelium, rod epithelium, serniniferous epithelium, sense epithelium,.
. .
. . .
gelatinous carcinoma, giant cell
carcinoma, gigantocellulare, glandular carcinoma, granulosa. cell carcinoma, hair-matrix
carcinoma, hematoid carcinoma, hepatocellular carcinoma (also called hepatoma, malignant
hepatoma and **hepatocarcinoma**), Mirthle cell carcinoma, hyaline carcinoma, hypernephroid
carcinoma, infantile embryonal carcinoma, carcinoma in situ, intraepidermal carcinoma,
intraepithelial carcinoma, Krompecher's carcinoma, Kulchitzky-cell carcinoma, lenticular
carcinoma,. . .
. . .
characterized by an abnormal mammalian cell proliferation to be treated by the methods of the invention include sarcomas. Sarcomas are rare **mesenchymal**

neoplasms that arise in bone and soft tissues. Different types of sarcomas are recognized and
these include: liposarcomas (including myxoid liposarcomas and pleiomorphic
liposarcomas), leiomyosarcomas, rhabdomyosarcomas, malignant peripheral nerve sheath
tumors (also called malignant schwannomas, neurofibrosarcomas, or neurogenic sarcomas),
Ewing's tumors (including **Ewing**'s **sarcoma** of bone,
extraskeletal [not bone] **Ewing**'s
io **sarcoma**, and primitive neuroectoderinal tumor [PNET]),
synovial sarcoma, angiosarconias,
hemangiosarcomas, lymphangiosarcomas, Kaposi's sarcoma,
hemangioendothelioma,
fibrosarcoma, desmoid tumor (also called aggressive fibromatosis),
dermatofibrosarcoma
protuberans (DFSP),. . .
. . .
immunostimulant peptides-, insulin-like growth factor-I receptor
inhibitoi, interferon
agonists; interferons; interleukins; iobenguane; lododoxorubicin;
1porneanol, 4-; irinotecan;
iroplact; irsogladine; isobengazole; isohomohalicondrin B; itasetron;
jasplakinolide;
kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin;
lenograstim; lentinan sulfate;
leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha
interferon; leuprolide +
estrogen + progesterone; leuprorelin;. . .

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=> d his

     (FILE 'HOME' ENTERED AT 16:12:12 ON 17 APR 2006)

     FILE 'PCTFULL' ENTERED AT 16:12:30 ON 17 APR 2006
L1           171 S JASPLAKINOLIDE
L2          1574 S EWING? (2W) SARCOMA
L3            36 S L2 AND L1
L4             1 S L3 NOT PY>2001
L5          5608 S HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL
L6             1 S L5 AND L4

=> s l5 and l1
L7           37 L5 AND L1

=> s l7 not py>2001
        488865 PY>2001
L8            4 L7 NOT PY>2001

=> d ibib 1-4

L8     ANSWER 1 OF 4      PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2001089520 PCTFULL  ED 20020826
TITLE (ENGLISH):         DEHYDROASCORBIC ACID FORMULATIONS AND USES THEREOF
TITLE (FRENCH):          FORMULATIONS D'ACIDE DEHYDROASCORBIQUE ET LEURS
                         UTILISATIONS
INVENTOR(S):             OLSON, William, C.;
                         ISRAEL, Robert, J.;
                         BOYD, Thomas, A.
PATENT ASSIGNEE(S):      PROGENICS PHARMACEUTICALS, INC.;
                         OLSON, William, C.;
                         ISRAEL, Robert, J.;
```

BOYD, Thomas, A.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001089520	A2	20011129

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2000-US41407 A 20001020
PRIORITY INFO.: US 2000-60/205,870 20000519

L8 ANSWER 2 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001029235 PCTFULL ED 20020820
TITLE (ENGLISH): TMS1 COMPOSITIONS AND METHODS OF USE
TITLE (FRENCH): COMPOSITIONS DU GENE TMS1 ET PROCEDES D'UTILISATION
INVENTOR(S): VERTINO, Paula, M.
PATENT ASSIGNEE(S): EMORY UNIVERSITY
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001029235	A2	20010426

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 2000-US28747 A 20001018
PRIORITY INFO.: US 1999-60/159,975 19991018

L8 ANSWER 3 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2000071135 PCTFULL ED 20020515
TITLE (ENGLISH): ANTI-TUMOR COMPRISING BOROPROLINE COMPOUNDS
TITLE (FRENCH): AGENTS ANTI-TUMORALES CONTENANT DES COMPOSES DE BOROPROLINE
INVENTOR(S): WALLNER, Barbara, P.;
MILLER, Glenn
PATENT ASSIGNEE(S): POINT THERAPEUTICS, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000071135	A1	20001130

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2000-US14505 A 20000525
PRIORITY INFO.: US 1999-60/135,861 19990525

L8 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999004817 PCTFULL ED 20020515

TITLE (ENGLISH): CHEMOTHERAPY SYNERGISTIC AGENT
TITLE (FRENCH): AGENT SYNERGIQUE POUR CHIMIOTHERAPIE
INVENTOR(S): WINKELMAN, James, W.;
BRIDGES, Kenneth, R.
PATENT ASSIGNEE(S): BRIGHAM & WOMEN'S HOSPITAL, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9904817	A1	19990204

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-US15052 A 19980722
PRIORITY INFO.: US 1997-60/053,696 19970725
US 1997-60/054,148 19970725

=> d kwic 4

L8 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . 91)
-
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcorna and osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basal. . .
. . .
peptides; insulin-like
growth factor-I receptor inhibitor; interferon agonists; interferons; interleukins; iobenguane;
I 0 iododoxorubicin; ipomeanol, 4-; irinotecan; iroplact; irsogladine; isobengazole;
isohomohalicondrin B; itasetron; **jasplakinolide**; kahalalide F;
larnellarin-N triacetate;
lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin; letrozole; leukemia
inhibiting factor; leukocyte alpha interferon; leuprolide + estrogen + progesterone;
leuprorelin;. . .

CLMEN. . . and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas, including
leiornyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basocellular. . .
. . .
and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squarnous cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal

cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin
- 24 -
cancer, including melanoma, Kaposi's. . .
. . .
and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer'; rectal cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basocellular. . .

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	15.65	15.86

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FILE COVERS 1907 - 17 Apr 2006 VOL 144 ISS 17
FILE LAST UPDATED: 16 Apr 2006 (20060416/ED)

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http://www.cas.org/infopolicy.html

=> s jasplakinolide/cn
REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L10 118 L9

=> s jasplakinolide
251 JASPLAKINOLIDE

```
            1 JASPLAKINOLIDES
L11       252 JASPLAKINOLIDE
                (JASPLAKINOLIDE OR JASPLAKINOLIDES)

=> s l11 or l10
L12       279 L11 OR L10

=> s hepatocarcinoma? or mesenchymal or neuroectodermal
         1409 HEPATOCARCINOMA?
        11238 MESENCHYMAL
         1281 NEUROECTODERMAL
L13     13848 HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL

=> s l13 and l12
L14          2 L13 AND L12

=> d ibib 1-2

L14  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2005:248055  CAPLUS
DOCUMENT NUMBER:         142:352644
TITLE:                   RhoA/ROCK Signaling Regulates Sox9 Expression and
                         Actin Organization during Chondrogenesis
AUTHOR(S):               Woods, Anita; Wang, Guoyan; Beier, Frank
CORPORATE SOURCE:        Canadian Institutes of Health Research Group in
                         Skeletal Development and Remodeling, Department of
                         Physiology and Pharmacology, University of Western
                         Ontario, London, ON, N6A 5C1, Can.
SOURCE:                  Journal of Biological Chemistry (2005), 280(12),
                         11626-11634
                         CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER:               American Society for Biochemistry and Molecular
                         Biology
DOCUMENT TYPE:           Journal
LANGUAGE:                English
REFERENCE COUNT:         73    THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2003:816528  CAPLUS
DOCUMENT NUMBER:         140:12638
TITLE:                   Two CD95 tumor classes with different sensitivities to
                         antitumor drugs
AUTHOR(S):               Algeciras-Schimnich, Alicia; Pietras, Eric M.;
                         Barnhart, Bryan C.; Legembre, Patrick; Vijayan,
                         Shrijay; Holbeck, Susan L.; Peter, Marcus E.
CORPORATE SOURCE:        The Ben May Institute for Cancer Research, University
                         of Chicago, Chicago, IL, 60637, USA
SOURCE:                  Proceedings of the National Academy of Sciences of the
                         United States of America (2003), 100(20), 11445-11450
                         CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:               National Academy of Sciences
DOCUMENT TYPE:           Journal
LANGUAGE:                English
REFERENCE COUNT:         26    THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> s ewing? (2W) sarcoma
         1659 EWING?
        36667 SARCOMA
         4162 SARCOMAS
          100 SARCOMATA
```

```
         38298 SARCOMA
                 (SARCOMA OR SARCOMAS OR SARCOMATA)
L15       1277 EWING? (2W) SARCOMA

=> s l15 and l12
L16          0 L15 AND L12

=> s dolastatin 11/cn
   REGISTRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.




L18         22 L17

=> s dolastatin 11
            390 DOLASTATIN
             59 DOLASTATINS
            404 DOLASTATIN
                  (DOLASTATIN OR DOLASTATINS)
         916607 11
L19         22 DOLASTATIN 11
                  (DOLASTATIN(W)11)

=> s l19 or l18
L20         24 L19 OR L18

=> d his

     (FILE 'HOME' ENTERED AT 16:12:12 ON 17 APR 2006)

     FILE 'PCTFULL' ENTERED AT 16:12:30 ON 17 APR 2006
L1           171 S JASPLAKINOLIDE
L2          1574 S EWING? (2W) SARCOMA
L3            36 S L2 AND L1
L4             1 S L3 NOT PY>2001
L5          5608 S HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL
L6             1 S L5 AND L4
L7            37 S L5 AND L1
L8             4 S L7 NOT PY>2001

     FILE 'CAPLUS' ENTERED AT 16:18:34 ON 17 APR 2006
                S JASPLAKINOLIDE/CN

     FILE 'REGISTRY' ENTERED AT 16:18:43 ON 17 APR 2006
L9             1 S JASPLAKINOLIDE/CN

     FILE 'CAPLUS' ENTERED AT 16:18:43 ON 17 APR 2006
L10          118 S L9
L11          252 S JASPLAKINOLIDE
L12          279 S L11 OR L10
L13        13848 S HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL
L14            2 S L13 AND L12
L15         1277 S EWING? (2W) SARCOMA
L16            0 S L15 AND L12
                S DOLASTATIN 11/CN

     FILE 'REGISTRY' ENTERED AT 16:20:17 ON 17 APR 2006
L17            1 S DOLASTATIN 11/CN
```

```
     FILE 'CAPLUS' ENTERED AT 16:20:18 ON 17 APR 2006
L18          22 S L17
L19          22 S DOLASTATIN 11
L20          24 S L19 OR L18

=> s l20 and l13
L21          1 L20 AND L13

=> d ibib

L21  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2003:816528  CAPLUS
DOCUMENT NUMBER:          140:12638
TITLE:                    Two CD95 tumor classes with different sensitivities to
                          antitumor drugs
AUTHOR(S):                Algeciras-Schimnich, Alicia; Pietras, Eric M.;
                          Barnhart, Bryan C.; Legembre, Patrick; Vijayan,
                          Shrijay; Holbeck, Susan L.; Peter, Marcus E.
CORPORATE SOURCE:         The Ben May Institute for Cancer Research, University
                          of Chicago, Chicago, IL, 60637, USA
SOURCE:                   Proceedings of the National Academy of Sciences of the
                          United States of America (2003), 100(20), 11445-11450
                          CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:                National Academy of Sciences
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          26    THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d kwic

L21  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
AB   . . . half are type II. Most of the type I cell lines fall into a
     distinct class of tumor cells expressing mesenchymal-like genes,
     whereas the type II cell lines preferentially express epithelium-like
     markers. This suggests that type I and II tumor cells represent different
     stages of carcinogenesis that resemble the epithelial-mesenchymal
     transition. We then screened the National Cancer Institute database of
     >42,000 compds. for reagents with patterns of growth inhibition that. .
     .
ST   soluble CD95ligand antitumor mesenchymal epithelial tumor actin
     tubulin disruption; antitumor resistance CD95 signaling gene expression
     carcinogenesis
IT   362-07-2, 2-Methoxyestradiol   1110-02-7, NSC 112167   2222-07-3,
     Cucurbitacin I   6040-19-3, Cucurbitacin A   6766-43-4, Cucurbitacin K
     33069-62-4D, Taxol, analog   82855-09-2D, Combretastatin, analog
     102396-24-7D, Jasplakinolide, analog   108675-64-5 111517-68-1,
     NSC 606195   141172-06-7   630400-59-8, NSC 666608   630400-60-1, NSC
     658831   630400-62-3, NSC 666606
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (two CD95 tumor classes with different sensitivities to antitumor
        drugs)
```

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PASSWORD:
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NEWS 3	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 8	JAN 30	Saved answer limit increased
NEWS 9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 14	FEB 28	TOXCENTER reloaded with enhancements
NEWS 15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 16	MAR 01	INSPEC reloaded and enhanced
NEWS 17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 18	MAR 08	X.25 communication option no longer available after June 2006
NEWS 19	MAR 22	EMBASE is now updated on a daily basis
NEWS 20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS 22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS 23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS 25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

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FILE 'HOME' ENTERED AT 09:03:09 ON 18 APR 2006

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FILE COVERS 1907 - 18 Apr 2006 VOL 144 ISS 17
FILE LAST UPDATED: 17 Apr 2006 (20060417/ED)

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http://www.cas.org/infopolicy.html

=> s cofilin
777 COFILIN
232 COFILINS
L1 814 COFILIN
(COFILIN OR COFILINS)

=> s inhibit?
L2 1822517 INHIBIT?

=> s l1 (L) l2
L3 221 L1 (L) L2

=> s hepatocar? or mesenchy? or nuroectoder? or (ewing?)
7077 HEPATOCAR?
15151 MESENCHY?
0 NUROECTODER?
1659 EWING?
L4 23829 HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)

=> s l3 and l4
L5 1 L3 AND L4

=> d ibib

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:977858 CAPLUS
DOCUMENT NUMBER: 138:52333
TITLE: Pharmaceutical composition for diagnosis, prevention or treatment of a tumorous state, comprising a modulator of the actin polymerization state
INVENTOR(S): Auclair, Christian; Amsellem, Valerie; Hervy, Martial; Subra, Frederic
PATENT ASSIGNEE(S): Bioalliance Pharma, Fr.; Ecole Normale Superieure De Cachan; Institut Gustave Roussy-IGR; Centre National de la Recherche Scientifique CNRS
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102846	A2	20021227	WO 2002-FR2106	20020618
WO 2002102846	A3	20040422		
WO 2002102846	B1	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2825928	A1	20021220	FR 2001-7976	20010618
FR 2825928	B1	20040402		
CA 2450845	AA	20021227	CA 2002-2450845	20020618
EP 1432732	A2	20040630	EP 2002-745538	20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005504521	T2	20050217	JP 2003-506318	20020618
US 2004191230	A1	20040930	US 2003-740266	20031218
PRIORITY APPLN. INFO.:			FR 2001-7976 A	20010618
			WO 2002-FR2106 W	20020618

```
=> s actin
         49687 ACTIN
         30340 ACTINS
L6       52687 ACTIN
                (ACTIN OR ACTINS)

=> s stabil?
L7     1026058 STABIL?

=> s l6 (l) l7
L8        2489 L6 (L) L7

=> d his

     (FILE 'HOME' ENTERED AT 09:03:09 ON 18 APR 2006)

     FILE 'CAPLUS' ENTERED AT 09:03:17 ON 18 APR 2006
L1           814 S COFILIN
L2       1822517 S INHIBIT?
```

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L3          221 S L1 (L) L2
L4        23829 S HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)
L5            1 S L3 AND L4
L6        52687 S ACTIN
L7      1026058 S STABIL?
L8         2489 S L6 (L) L7

=> s l8 and l4
L9           19 L8 AND L4

=> s l9 not py>2002
       3759065 PY>2002
L10           8 L9 NOT PY>2002

=> s l9 not py>2001
       4742175 PY>2001
L11           8 L9 NOT PY>2001

=> d ibib 1-8

L11  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2002:88952  CAPLUS
DOCUMENT NUMBER:          136:242165
TITLE:                    TGFβ is required for the formation of
                          capillary-like structures in three-dimensional
                          cocultures of 10T1/2 and endothelial cells
AUTHOR(S):                Darland, D. C.; D'Amore, P. A.
CORPORATE SOURCE:         The Schepens Eye Research Institute and the Department
                          of Ophthalmology, Harvard Medical School, Boston, MA,
                          02114, USA
SOURCE:                   Angiogenesis (2001), 4(1), 11-20
                          CODEN: AGIOFT; ISSN: 0969-6970
PUBLISHER:                Kluwer Academic Publishers
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          51    THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11  ANSWER 2 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2001:7412  CAPLUS
DOCUMENT NUMBER:          134:264229
TITLE:                    Integrin α3β1 engagement disrupts
                          intercellular adhesion
AUTHOR(S):                Kawano, Kenji; Kantak, Seema S.; Murai, Mutsuhiko;
                          Yao, Chung-Chen; Kramer, Randall H.
CORPORATE SOURCE:         Department of Stomatology, University of California at
                          San Francisco, San Francisco, CA, 94143-0512, USA
SOURCE:                   Experimental Cell Research (2001), 262(2), 180-196
                          CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER:                Academic Press
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          66    THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11  ANSWER 3 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2000:336418  CAPLUS
DOCUMENT NUMBER:          133:87270
TITLE:                    The tetraspan molecule CD151, a novel constituent of
                          hemidesmosomes, associates with the integrin
                          α6β4 and may regulate the spatial
                          organization of hemidesmosomes
AUTHOR(S):                Sterk, Lotus M. Th.; Geuijen, Cecile A. W.; Oomen,
```

Lauran C. J. M.; Calafat, Jero; Janssen, Hans; Sonnenberg, Arnoud
CORPORATE SOURCE: Division of Cell Biology, The Netherlands Cancer Institute, Amsterdam, 1066 CX, Neth.
SOURCE: Journal of Cell Biology (2000), 149(4), 969-982
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:517212 CAPLUS
DOCUMENT NUMBER: 129:170359
TITLE: Expression of human bone morphogenic protein 7 in primary rabbit periosteal cells. Potential utility in gene therapy for osteochondral repair
AUTHOR(S): Mason, J. M.; Grande, D. A.; Barcia, M.; Grant, R.; Pergolizzi, R. G.; Breitbart, A. S.
CORPORATE SOURCE: Viral Vector Lab., Dep. Res., North Shore Univ. Hosp.-New York Univ. Sch. Med., Manhasset, NY, 11030, USA
SOURCE: Gene Therapy (1998), 5(8), 1098-1104
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:269919 CAPLUS
DOCUMENT NUMBER: 126:260361
TITLE: Modulation of LDL receptor mRNA stability by phorbol esters in human liver cell culture models
AUTHOR(S): Wilson, G. M.; Roberts, E. A.; Deeley, R. G.
CORPORATE SOURCE: Department of Biochemistry and Cancer Research Laboratories, Queen's University, Kingston, ON, Can.
SOURCE: Journal of Lipid Research (1997), 38(3), 437-446
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:145098 CAPLUS
DOCUMENT NUMBER: 116:145098
TITLE: Gene regulatory factors of the sea urchin embryo. I. Purification by affinity chromatography and cloning of P3A2, a novel DNA-binding protein
AUTHOR(S): Calzone, Frank J.; Hoeoeg, Christer; Teplow, David B.; Cutting, Ann E.; Zeller, Robert W.; Britten, Roy J.; Davidson, Eric H.
CORPORATE SOURCE: Div. Biol., California Inst. Technol., Pasadena, CA, 91125, USA
SOURCE: Development (Cambridge, United Kingdom) (1991), 112(1), 335-50
CODEN: DEVPED; ISSN: 0950-1991
DOCUMENT TYPE: Journal
LANGUAGE: English

L11 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:595544 CAPLUS
DOCUMENT NUMBER: 107:195544
TITLE: Developmental and tissue-specific regulation of β-tubulin gene expression in the embryo of the sea urchin Strongylocentrotus purpuratus
AUTHOR(S): Harlow, Patricia; Nemer, Martin
CORPORATE SOURCE: Inst. Cancer Res., Fox Chase Cancer Cent., Philadelphia, PA, 19111, USA
SOURCE: Genes & Development (1987), 1(2), 147-60
CODEN: GEDEEP; ISSN: 0890-9369
DOCUMENT TYPE: Journal
LANGUAGE: English

L11 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:140906 CAPLUS
DOCUMENT NUMBER: 98:140906
TITLE: A yellow crescent cytoskeletal domain in ascidian eggs and its role in early development
AUTHOR(S): Jeffery, William R.; Meier, Stephen
CORPORATE SOURCE: Dep. Zool., Univ. Texas, Austin, TX, 78712, USA
SOURCE: Developmental Biology (Orlando, FL, United States) (1983), 96(1), 125-43
CODEN: DEBIAO; ISSN: 0012-1606
DOCUMENT TYPE: Journal
LANGUAGE: English

=> d kwic 3

L11 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AB . . . and certain integrins to form large complexes at the cell surface. CD151 is expressed by a variety of epithelia and **mesenchymal** cells. We demonstrate here that in human skin CD151 is codistributed with α3β1 and α6β4 at the basolateral surface of. . . cell surface in association with patches of laminin-5. Focal adhesions are present at the periphery of these clusters, connected with **actin** filaments, and they contain both CD151 and α3β1. Transient transfection studies of PA-JEB cells with β4 revealed that the integrin. . . recruitment into hemidesmosomes is regulated by the integrin α6β4. We suggest that CD151 plays a role in the formation and **stability** of hemidesmosomes by providing a framework for the spatial organization of the different hemidesmosomal components.

=> s dolastatin or jasplakinolide
390 DOLASTATIN
59 DOLASTATINS
404 DOLASTATIN
(DOLASTATIN OR DOLASTATINS)
251 JASPLAKINOLIDE
1 JASPLAKINOLIDES
252 JASPLAKINOLIDE
(JASPLAKINOLIDE OR JASPLAKINOLIDES)
L12 652 DOLASTATIN OR JASPLAKINOLIDE

=> d his

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FILE 'CAPLUS' ENTERED AT 09:03:17 ON 18 APR 2006

```
L1          814 S COFILIN
L2      1822517 S INHIBIT?
L3          221 S L1 (L) L2
L4        23829 S HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)
L5            1 S L3 AND L4
L6        52687 S ACTIN
L7      1026058 S STABIL?
L8         2489 S L6 (L) L7
L9           19 S L8 AND L4
L10           8 S L9 NOT PY>2002
L11           8 S L9 NOT PY>2001
L12         652 S DOLASTATIN OR JASPLAKINOLIDE

=> s l12 and l4
L13           8 L12 AND L4

=> s l13 not py>2001
       4742175 PY>2001
L14           0 L13 NOT PY>2001

=> s l13 not py>2002
       3759065 PY>2002
L15           0 L13 NOT PY>2002

=> d l13 ibib 1-8

L13  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:13464  CAPLUS
DOCUMENT NUMBER:          144:101073
TITLE:                    therapeutic uses of kinase inhibitors, and
                          compositions thereof
INVENTOR(S):              Caligiuri, Maureen G.; Kley, Nikolai A.; Murthi,
                          Krishna K.
PATENT ASSIGNEE(S):       GPC Biotech, Inc., USA
SOURCE:                   PCT Int. Appl., 201 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2006002119         A2    20060105    WO 2005-US21843         20050617
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM,
             KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG,
             KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                        US 2004-580868P     P  20040618
OTHER SOURCE(S):          MARPAT 144:101073

L13  ANSWER 2 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:1290072  CAPLUS
DOCUMENT NUMBER:          144:46998
TITLE:                    The X-ray crystal structure of BRCA1 tandem BRCT
```

repeat and BACH1 phosphopeptide complex and methods and compositions for antitumor drug design

INVENTOR(S): Yaffe, Michael B.; Clapperton, Julie A.; Manke, Isaac A.; Lowery, Drew M.; Ho, Timmy; Haire, Lesley F.; Smerdon, Stephen J.

PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA

SOURCE: PCT Int. Appl., 360 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005115454	A2	20051208	WO 2005-US15981	20050509

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-569131P P 20040507

L13 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:409543 CAPLUS

DOCUMENT NUMBER: 142:457053

TITLE: Human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy

INVENTOR(S): Lacasse, Eric; McManus, Daniel

PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.

SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042558	A1	20050512	WO 2004-CA1902	20041029

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005148535	A1	20050707	US 2004-975974	20041028

PRIORITY APPLN. INFO.: US 2003-516192P P 20031030

L13 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409357 CAPLUS
DOCUMENT NUMBER: 142:457052
TITLE: Sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with a chemotherapeutic agent
INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042030	A1	20050512	WO 2004-CA1900	20041029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005119217	A1	20050602	US 2004-975790	20041028
PRIORITY APPLN. INFO.:			US 2003-516263P P	20031030

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:283298 CAPLUS
DOCUMENT NUMBER: 142:349042
TITLE: Combinations of chlorpromazine compounds and antiproliferative drugs for the treatment of neoplasms
INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen; Keith, Curtis
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916
WO 2005027842	A3	20051222		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,				

SN, TD, TG
PRIORITY APPLN. INFO.: US 2003-504310P P 20030918
OTHER SOURCE(S): MARPAT 142:349042

L13 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:248055 CAPLUS
DOCUMENT NUMBER: 142:352644
TITLE: RhoA/ROCK Signaling Regulates Sox9 Expression and Actin Organization during Chondrogenesis
AUTHOR(S): Woods, Anita; Wang, Guoyan; Beier, Frank
CORPORATE SOURCE: Canadian Institutes of Health Research Group in Skeletal Development and Remodeling, Department of Physiology and Pharmacology, University of Western Ontario, London, ON, N6A 5C1, Can.
SOURCE: Journal of Biological Chemistry (2005), 280(12), 11626-11634
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:816528 CAPLUS
DOCUMENT NUMBER: 140:12638
TITLE: Two CD95 tumor classes with different sensitivities to antitumor drugs
AUTHOR(S): Algeciras-Schimnich, Alicia; Pietras, Eric M.; Barnhart, Bryan C.; Legembre, Patrick; Vijayan, Shrijay; Holbeck, Susan L.; Peter, Marcus E.
CORPORATE SOURCE: The Ben May Institute for Cancer Research, University of Chicago, Chicago, IL, 60637, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(20), 11445-11450
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:924095 CAPLUS
DOCUMENT NUMBER: 136:31647
TITLE: Toxicity typing using **mesenchymal** stem cells
INVENTOR(S): Snodgrass, H. Ralph
PATENT ASSIGNEE(S): Vistagen, Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096865	A1	20011220	WO 2001-US19048	20010614

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,

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            RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
            UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
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            BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2412769           AA    20011220    CA 2001-2412769         20010614
     US 2002045179        A1    20020418    US 2001-881475          20010614
     EP 1290443           A1    20030312    EP 2001-946335          20010614
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004503255        T2    20040205    JP 2002-510943          20010614
PRIORITY APPLN. INFO.:                      US 2000-211608P     P   20000614
                                            WO 2001-US19048     W   20010614
REFERENCE COUNT:         7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> file pctfull
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   51.50      51.71

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -0.75      -0.75

FILE 'PCTFULL' ENTERED AT 09:07:34 ON 18 APR 2006
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FILE LAST UPDATED:         11 APR 2006      <20060411/UP>
MOST RECENT UPDATE WEEK:       200614        <200614/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
    SEE
    http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE
    (last updated April 10, 2006) <<<

=> s dolastatin or jasplakinolide
           459 DOLASTATIN
            70 DOLASTATINS
           477 DOLASTATIN
                 (DOLASTATIN OR DOLASTATINS)
           171 JASPLAKINOLIDE
             1 JASPLAKINOLIDES
           171 JASPLAKINOLIDE
                 (JASPLAKINOLIDE OR JASPLAKINOLIDES)
L16        643 DOLASTATIN OR JASPLAKINOLIDE

=> s hepatocar? or mesenchy? or nuroectoder? or (ewing?)
           770 HEPATOCAR?
          5688 MESENCHY?
             0 NUROECTODER?
          3185 EWING?
L17       8782 HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)

=> s l17 and l16
L18        243 L17 AND L16
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=> s l18 not py>2001
        488865 PY>2001
L19         16 L18 NOT PY>2001

=> s l16/clm
            60 DOLASTATIN/CLM
             7 JASPLAKINOLIDE/CLM
L20         67 (DOLASTATIN/CLM OR JASPLAKINOLIDE/CLM)

=> s l20 and l19
L21          0 L20 AND L19

=> s l19 not py>2000
        587352 PY>2000
L22          8 L19 NOT PY>2000

=> d ibib 1-8

L22    ANSWER 1 OF 8     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2000071135 PCTFULL  ED 20020515
TITLE (ENGLISH):         ANTI-TUMOR COMPRISING BOROPROLINE COMPOUNDS
TITLE (FRENCH):          AGENTS ANTI-TUMORALES CONTENANT DES COMPOSES DE
                         BOROPROLINE
INVENTOR(S):             WALLNER, Barbara, P.;
                         MILLER, Glenn
PATENT ASSIGNEE(S):      POINT THERAPEUTICS, INC.
LANGUAGE OF PUBL.:       English
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 2000071135         A1 20001130
DESIGNATED STATES
       W:                AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ
                         DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
                         JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
                         MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
                         TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ
                         TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK
                         ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM
                         GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:       WO 2000-US14505       A  20000525
PRIORITY INFO.:          US 1999-60/135,861       19990525

L22    ANSWER 2 OF 8     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2000067802 PCTFULL  ED 20020515
TITLE (ENGLISH):         FATTY ACID-N-SUBSTITUTED INDOL-3-GLYOXYL-AMIDE
                         COMPOSITIONS AND USES THEREOF
TITLE (FRENCH):          COMPOSITIONS D'ACIDES GRAS -N-SUBSTITUTED
                         INDOL-3-GLYOXYL-AMIDE ET LEUR UTILISATION
INVENTOR(S):             BRADLEY, Matthews, O.;
                         SWINDELL, Charles, S.;
                         ANTHONY, Forrest;
                         WEBB, Nigel, L.;
                         FISHER, Mark
PATENT ASSIGNEE(S):      PROTARGA, INC.
LANGUAGE OF PUBL.:       English
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 2000067802         A1 20001116
DESIGNATED STATES
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W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG
ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI
FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN
GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US12752 A 20000510
PRIORITY INFO.: US 1999-60/133,292 19990510

L22 ANSWER 3 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2000064946 PCTFULL ED 20020515
TITLE (ENGLISH): COMPOSITIONS AND METHODS FOR CANCER TREATMENT BY SELECTIVELY INHIBITING VEGF
TITLE (FRENCH): COMPOSITIONS ET PROCEDES DE TRAITEMENT DU CANCER PAR INHIBITION SELECTIVE DE VEGF
INVENTOR(S): THORPE, Philip, E.;
BREKKEN, Rolf, A.
PATENT ASSIGNEE(S): BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000064946	A2	20001102

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG
ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI
FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN
GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US11367 A 20000428
PRIORITY INFO.: US 1999-60/131,432 19990428

L22 ANSWER 4 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2000050016 PCTFULL ED 20020515
TITLE (ENGLISH): COMPOSITIONS AND METHODS FOR IMPROVING INTEGRITY OF COMPROMISED BODY PASSAGEWAYS AND CAVITIES
TITLE (FRENCH): COMPOSITIONS ET METHODES POUR L'AMELIORATION DE L'INTEGRITE DE CAVITES ET DE PASSAGES CORPORELS AFFAIBLIS
INVENTOR(S): SIGNORE, Pierre, E.;
MACHAN, Lindsay, S.
PATENT ASSIGNEE(S): ANGIOTECH PHARMACEUTICALS, INC.;
SIGNORE, Pierre, E.;
MACHAN, Lindsay, S.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000050016	A2	20000831

DESIGNATED STATES
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE
DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE
KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX
NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA
UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW
AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR

GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2000-CA175 A 20000223
PRIORITY INFO.: US 1999-60/121,424 19990223

L22 ANSWER 5 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999062510 PCTFULL ED 20020515
TITLE (ENGLISH): COMPOSITIONS COMPRISING ANTI-MICROTUBULE AGENTS FOR TREATING OR PREVENTING INFLAMMATORY DISEASES
TITLE (FRENCH): COMPOSITIONS RENFERMANT DES AGENTS ANTI-MICROTUBULES POUR LE TRAITEMENT OU LA PREVENTION DE MALADIES INFLAMMATOIRES
INVENTOR(S): HUNTER, William, L.
PATENT ASSIGNEE(S): ANGIOTECH PHARMACEUTICALS, INC.;
HUNTER, William, L.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9962510	A2	19991209

DESIGNATED STATES
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 1999-CA464 A 19990601
PRIORITY INFO.: US 1998-09/088,546 19980601

L22 ANSWER 6 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999055343 PCTFULL ED 20020515
TITLE (ENGLISH): CNRE BINDING FACTORS AND USES THEREOF
TITLE (FRENCH): FACTEURS DE LIAISON CNRE ET UTILISATIONS CORRESPONDANTES
INVENTOR(S): CHEN, Yuqing, E.;
HORIUCHI, Masatsugu;
DZAU, Victor, J.;
TAMURA, Koichi
PATENT ASSIGNEE(S): THE BRIGHAM AND WOMEN'S HOSPITAL, INC.;
CHEN, Yuqing, E.;
HORIUCHI, Masatsugu;
DZAU, Victor, J.;
TAMURA, Koichi
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9955343	A1	19991104

DESIGNATED STATES
W: CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1999-US8502 A 19990423
PRIORITY INFO.: US 1998-60/082,997 19980424

L22 ANSWER 7 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999004817 PCTFULL ED 20020515
TITLE (ENGLISH): CHEMOTHERAPY SYNERGISTIC AGENT
TITLE (FRENCH): AGENT SYNERGIQUE POUR CHIMIOTHERAPIE
INVENTOR(S): WINKELMAN, James, W.;

BRIDGES, Kenneth, R.
PATENT ASSIGNEE(S): BRIGHAM & WOMEN'S HOSPITAL, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9904817	A1	19990204

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-US15052 A 19980722
PRIORITY INFO.: US 1997-60/053,696 19970725
US 1997-60/054,148 19970725

L22 ANSWER 8 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1998035554 PCTFULL ED 20020514
TITLE (ENGLISH): COMBINED TUMOR SUPPRESSOR GENE THERAPY AND CHEMOTHERAPY IN THE TREATMENT OF NEOPLASMS
TITLE (FRENCH): COMBINAISON THERAPIE GENIQUE SUPPRESSIVE DE TUMEURS - CHIMIOTHERAPIE UTILISEE DANS LE TRAITEMENT DE NEOPLASMES
INVENTOR(S): NIELSEN, Loretta;
HOROWITZ, Jo, Ann;
MANEVAL, Daniel, C.;
DEMERS, G., William;
RYBAK, Mary, Ellen;
RESNICK, Gene
PATENT ASSIGNEE(S): CANJI, INC.;
NIELSEN, Loretta;
HOROWITZ, Jo, Ann;
MANEVAL, Daniel, C.;
DEMERS, G., William;
RYBAK, Mary, Ellen;
RESNICK, Gene
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9835554	A2	19980820

DESIGNATED STATES
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.: WO 1998-US3514 A 19980217
PRIORITY INFO.: US 1997-8/801,285 19970218
US 1997-8/801,681 19970218
US 1997-8/801,755 19970218
US 1997-8/801,765 19970218
US 1997-60/038,065 19970218
US 1997-60/047,834 19970528

=> d kwic 5, 7

L22 ANSWER 5 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . subtilisin, 1069C85, steganacin, combretastatin, curacin,

estradiol,
2-methoxyestradiol, flavanol, rotenone, griseofulvin, vinca alkaloids, including
vinblastine and vincristine, maytansinoids and ansamitocins, rhizoxin, phornopsin A,
ustiloxins, **dolastatin** 10, **dolastatin** 15,
halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam. betaine. taurine, isethionate, HO-221, adociasulfate-2,
estramustine, monoclonal anti-idiotypic antibodies, microtubule assembly promoting
protein (taxol-like protein, TALP),. . .
. . .
phomopsin A (Hamel, Med. Res. Rev. 16(2): 207-23) 1, 1996), ustiloxins
(Hamel, Med Res. Rev. 16(2): 207-23) 1, 1996), **dolastatin** I 0
(Hamel, Med. Res. Rev.

16(2): 207-23) 1, 1996). **dolastatin** 15 (Hamel. Med Res. Rev.
16(2): 207-23) 1, 1996),
halichondrins and halistatins (Hamel, Med. Res. Rev. 16(2): 207-231,
1996),
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subtilisin,
1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol, flavanol,
rotenone, griseofulvin, vinca alkaloids, including vinblastine and
vincristine,
maytansinoids and ansamitocins, rhizoxin. phomopsin A. ustiloxins,
dolastatin 10,
dolastatin 15, halichondrins and halistatins, spongistatins.
cryptophycins, rhazinilam,
betaine, taurine, isethionate. HO-221, adociasulfate-2, estramustine.
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein
(taxol-like. . .
. . .
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rotenone, griseofulvin, vinca alkaloids, including vinblastine and
vincristine,
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betaine, taurine, isethionate, HO-221, adociasulfate-2, estrainustine.
monoclonal anti-
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(taxol-like. . .
. . .
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1069C85. steganacin. combretastatin. curacin, estradiol,
2-methoxyestradiol. flavanol,
rotenone, griseofulvin, vinca alkaloids. including vinblastine and
vincristine,
maytansinoids and ansamitocins, rhizoxin. phornopsin A, ustiloxins.
dolastatin 10,
dolastatin 15. halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilarn,
betaine, taurine, isethionate, HO-221, adociasulfate-2, estramustine,
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein

(taxol-like. . .
. . .
subtilisin,
1069C85. steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol, flavanol,
rotenone. griseofulvin, vinca alkaloids, including vinblastine and
vincristine,
maytansinoids and ansamitocins, rhizoxin, phomopsin A, ustiloxins,
dolastatin 10.

dolastatin 15, halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam,
betaine, taurine, isethionate, HO-221, adociasulfate-2, estramustine,
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein
(taxol-like. . .
. . .
subtilisin. 1069C85, steganacin,
combretastatin, curacin, estradiol, 2-methoxyestradiol, flavanol,
rotenone, griseofulvin,
vinca alkaloids. including vinblastine and vincristine, maytansinoids
and ansamitocins,
rhizoxin, phomopsin A. ustiloxins, **dolastatin** 10.
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dolastatin I 0,
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microtubule
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. . .
endpoints: (1) inhibition of
the white blood cell response (macrophages, neutrophils and T cells)
which initiates the
inflammatory cascade; (2) inhibition of **mesenchyrnal** cell
(fibroblasts, synoviocytes,
etc.) hyperproliferation that leads to the development of fibrosis and
loss of organ
function; (3) inhibition of matrix metalloproteinase. . .

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DETD . . . 91)
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lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous
cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal
cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal
cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcorna and
osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basal. . .
. . .
peptides; insulin-like
growth factor-I receptor inhibitor; interferon agonists; interferons;
interleukins; iobenguane;
I 0 iododoxorubicin; ipomeanol, 4-; irinotecan; iroplact; irsogladine;
isobengazole;
isohomohalicondrin B; itasetron; **jasplakinolide**; kahalalide F;
larnellarin-N triacetate;
lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin;
letrozole; leukemia
inhibiting factor; leukocyte alpha interferon; leuprolide + estrogen +
progesterone;
leuprorelin;. . .

CLMEN. . . and
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cell carcinoma;
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cells, germ cells and
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cancer, including melanoma, Kaposi's sarcoma, basocellular. . .
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mesenchymal cells; pancreas cancer; prostate cancer; rectal
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leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and
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- 24 -
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